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ABSTRACT

This publication summarizes current knowledge about Acquired Immunodeficiency Syndrome (AIDS) in children and recommends future directions for research, prevention, and amelioration of the effects of pediatric AIDS. After an excerpt from Surgeon General Koop's keynote address, contents provide selections from workshop presentations concerning (1) the global epidemiology of AIDS; (2) the Human Immunodeficiency Virus (HIV); (3) the immunology of pediatric AIDS; (4) transmission of HIV in the United States; (5) approaches to prevention of HIV infection; (6) the natural history of HIV infection in children; (7) HIV transmitted by blood products; (8) supportive care and treatment of pediatric AIDS; (9) intravenous drug abuse and women's medical issues; (10) education to prevent HIV infection; (11) legal issues surrounding medical care, treatment, and research on children; (12) management of the child with HIV infection, with implications for service delivery; (13) developments in and prospects for AIDS vaccines; and (14) a mother's viewpoint on the needs of families of children with AIDS. Recommendations of 10 work groups, each of which focused on a specific set of issues, and the response of the Surgeon General are offered. Appendices provide related materials, such as guidelines for management of HIV, a list of selected readings, and a classification system for HIV infection in children under 13 years of age. (RH)

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Report of The Surgeon General's Workshop on Children With HIV Infection And Their Families

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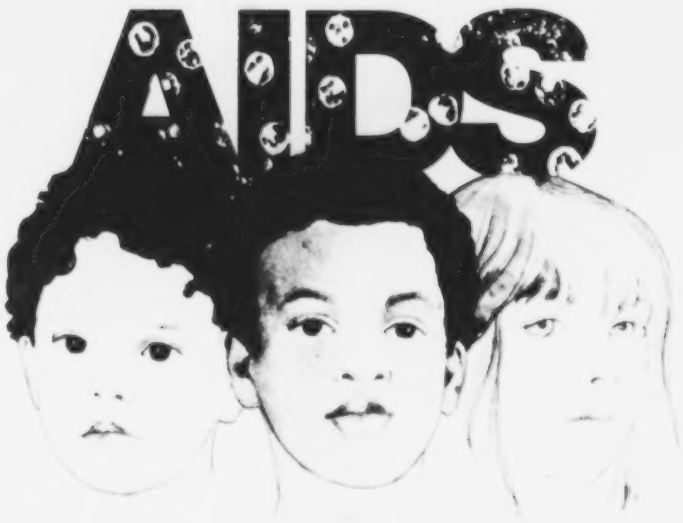
"I am the Surgeon General of the heterosexuals and the homosexuals, of the young and the old, of the moral or the immoral, the married and the unmarried. I don't have the luxury of deciding which side I want to be on."

—C. Everett Koop
The Washington Post Health Magazine
24 March 1987

Report of The Surgeon General's Workshop on Children With HIV Infection And Their Families



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Division of Maternal and Child Health

In conjunction with
The Children's Hospital of Philadelphia

April 6th-9th, 1987

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This book is dedicated to the memory of Samuel Jared Kushnick in testimony of how much "his life has counted" and how well "his voice is heard."

The Surgeon General's Workshop on
Children with HIV Infection and Their Families
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This report was edited by
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The photograph of the AIDS virus used in the logo was taken by Mr. Robert J. Munn, Department of Pathology, School of Medicine, University of California, Davis, CA 95616

PREFACE

This Surgeon General's Workshop on Children with HIV Infection and Their Families provides an opportunity to summarize the current knowledge about AIDS (Acquired Immunodeficiency Syndrome) in children and to make recommendations about future directions in research, prevention, and amelioration of the effects of pediatric AIDS. Surgeon General's Workshops, of which this is the fifth, have been useful vehicles for assembling experts to improve the health of mothers and children. Representatives of major professional and voluntary organizations and from various components of the Department of Health and Human Services insure not only a comprehensive coverage of the subject but also a network to disseminate and implement the recommendations.

In the early eighties we realized that children could develop AIDS when it became apparent that this then very mysterious disease could be transmitted by blood transfusions and the administration of blood products to treat hemophilia. Initially it was difficult to distinguish this entity from the rare and puzzling congenital immunodeficiency diseases in children.

By 1984 the numbers of children with AIDS had begun to escalate, especially in New York City, Newark, and Miami. The Division of Maternal and Child Health first held an ad hoc meeting to try to delineate the nature of the problem in NYC where infants were occupying acute care hospital beds unnecessarily because no alternative living arrangements were available. DMCH joined other departmental groups in cosponsoring the first National Meeting on Pediatric AIDS in November, 1984. Attendees at this meeting agreed that AIDS *did* occur in children, that the number of children involved was undercounted in the CDC surveillance system, and that infected infants and children and their families were subject to discrimination and sometimes barred from basic services. Participants expressed concern about seemingly insoluble problems, although some told of initial efforts to solve them.

DMCH, the New York State Health Department, and the Albert Einstein College of Medicine cosponsored a second National Pediatric AIDS Meeting held in March, 1986. A larger group—predominantly of physicians but also of other health workers, child welfare workers, and educators—exchanged information about the clinical spectrum and treatment efforts. A new confidence resulted from the increasing knowledge about the etiology and transmission of AIDS. We recognized that many generic solutions were applicable to HIV infection. Many could remember when most infections could be managed even without vaccines and antibiotics. It has been especially heartening to hear how the State Health Department, the Hemophilia Treatment Center, and the local school had worked together in Swansea, Massachusetts, to retain a boy with AIDS in school in a manner that evoked the best instincts of his classmates and their families.

This, then, is actually the third national meeting on pediatric AIDS, and is conducted as a Surgeon General's Workshop to bring our best efforts to bear against this new disease.

C. Everett Koop, M.D., Sc.D.
Surgeon General

PLANNING COMMITTEE

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Department of Pediatrics

Benjamin K. Silverman, M.D.
Department of Emergency Medicine

WORKSHOP PROGRAM

Monday, April 6, 1987

	Plenary Session The Children's Hospital of Philadelphia
Greetings	John Hutchings, M.D. Assistant Director Division of Maternal and Child Health Department of Health and Human Services Rockville, MD
Presiding	Stanley A. Plotkin, M.D. Director, Division of Infectious Diseases The Children's Hospital of Philadelphia
Welcome	Edmond F. Notebaert, President and Chief Executive Officer The Children's Hospital Foundation The Children's Hospital of Philadelphia
	Robert Zimmerman, M.P.H. Acting Deputy Secretary for Public Health Programs Pennsylvania State Department of Health
	Harriett Williams Deputy Commissioner for Community Health Services City of Philadelphia
Keynote and Charge	C. Everett Koop, M.D., Sc.D. Surgeon General Public Health Service Department of Health and Human Services
Global Epidemiology	Thomas C. Quinn, M.D., M.S. National Institute of Allergy and Infectious Diseases Associate Professor of Medicine Johns Hopkins University, Baltimore, MD
The Human Immunodeficiency Virus	Wade P. Parks, M.D., Ph.D. Director of Pediatrics Division of Immunology and Infectious Disease University of Miami School of Medicine Miami, FL
Immunology of HIV Infection	Arthur J. Ammann, M.D. Director, Collaborative Research Genentech, Inc. South San Francisco, CA
Epidemiology and Transmission of Pediatric Infection	Martha F. Rogers, M.D. AIDS Program/Center for Infectious Diseases Centers for Disease Control Atlanta, GA
Approaches to Prevention of HIV Infection	Walter R. Dowdle, Ph.D. Acting Deputy Director (AIDS) Centers for Disease Control Atlanta, GA
Natural History of HIV Infection I	Gwendolyn B. Scott, M.D. Associate Professor of Pediatrics Head, Division of Infectious Disease and Immunology University of Miami School of Medicine Miami, FL
Natural History of HIV Infection II	James Oleske, M.D. Associate Professor Department of Pediatrics College of Medicine and Dentistry of New Jersey Newark, NJ

Tuesday, April 7, 1987

Plenary Session Continued

HIV Transmitted by Blood Products

Margaret W. Hilgartner, M.D.
Professor of Pediatrics
Director, Division of Pediatric Hematology/Oncology
New York Hospital-Cornell Medical Center
New York, NY

Supportive Treatment of Pediatric HIV Infection

Arye Rubenstein, M.D.
Professor of Pediatrics, Microbiology and Immunology
Albert Einstein College of Medicine of Yeshiva University
Bronx, NY

Drug Abuse and Women's Medical Issues

Constance B. Wofsy, M.D.
Co-Director, AIDS Activities
Principal Investigator, Project AWARE
San Francisco General Hospital
San Francisco, CA

Education to Prevent HIV Infection

Karolynn Siegel, Ph.D.
Director of Research
Department of Social Work
Memorial Sloan Kettering Cancer Center
New York, NY

Legal Issues

Harold M. Ginzburg, M.D., J.D., M.P.H.
Chief, Epidemiology Branch
AIDS Program
National Institute of Allergy and Infectious Diseases
Bethesda, MD

Management of Children with HIV Infection

Mary Boland, R.N., M.S.N., C.P.N.P.
Director, AIDS Program
Children's Hospital of New Jersey
Newark, NJ

Vaccine Strategies

Gerald V. Quinnan, Jr., M.D.
Division of Virology
Office of Biologics Research and Review
Center for Drugs and Biologics
Food and Drug Administration
Bethesda, MD

A Mother's Viewpoint

Helen G. Kushnick
General Management Corporation
Los Angeles, CA

Individual Work Groups Begin

Wednesday, April 8, 1987

Individual Work Group Recommendations

Plenary Session: Work Groups' Summation and Presentation

Surgeon General's Response

C. Everett Koop, M.D., Sc.D.

Close

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COMMONWEALTH OF PENNSYLVANIA
OFFICE OF THE GOVERNOR
HARRISBURG

GREETINGS:

As Governor of the Commonwealth of Pennsylvania, it gives me great pleasure to extend greetings to all those gathered for the AIDS workshop being held by United States Surgeon General, Dr. C. Everett Koop, M.D. at The Children's Hospital of Philadelphia.

I applaud all of you for the dedicated and professional efforts you have taken to improve and strengthen pediatric health care.

Best wishes for a productive and meaningful workshop.

Robert P. Casey
Governor

X

INTRODUCTION

AIDS in children has been a sensational but little understood issue. Fear and ignorance have impeded efforts to understand and control the AIDS epidemic in adults, and this has been even more true for children. Children acquire AIDS as a consequence of adult behavior, but they nevertheless have shared general public opprobrium frequently cast on affected patients.

As of 30 March 1987, a cumulative total of 471 children nationwide met the strict criteria established by the Centers for Disease Control (CDC) for Acquired Immunodeficiency Syndrome (AIDS) in children. An untold additional number, perhaps two to three times more, are infected with the Human Immunodeficiency Virus (HIV) but do not meet the CDC criteria. It is not generally appreciated that AIDS is only one of the more severe manifestations of infection with HIV. Other children infected with HIV may fall anywhere on a spectrum from being completely asymptomatic through suffering growth and developmental retardation to having multisystem disease known as AIDS-Related Complex (ARC) involving blood, skin, brain, heart, kidneys, and other organs.

Both future opportunities for control of HIV infection and the possibilities for future disaster lie in the area of heterosexually transmitted infections in adults and their consequences to children. At present, pediatric infections – other than those acquired previously through HIV contaminated blood products – stem largely from mothers who themselves are intravenous drug users or whose partners either abuse drugs or are bisexual. If the virus continues to spread through these groups, there inevitably will be more heterosexual infections and more transmission to infants, both within and without the drug using and bisexual sectors.

The idea for this conference arose from our perception that the attention of the nation needed to be focused on prevention of HIV infection in children and on the difficulties of caring for those children already infected. At the same time, we learned that the Surgeon General was considering convening a workshop specifically to deal with issues arising from pediatric AIDS. Accordingly, a series of meetings took place in the summer and fall of 1986 to plan for a conference. In the subsequent months, approximately 200 people were invited to a closed conference, known as the "Surgeon General's Workshop on Children with HIV Infection and Their Families."

We made a deliberate effort to convene not only clinical and research physicians, but other types of health providers, clergy, economists, educators, media representatives, and parents. Due attention was given to ethnic and geographical representation.

The workshop took place at Children's Hospital of Philadelphia on 6–8 April, 1987. The fifteen papers surveying what is known in the field were presented in plenary session. Following are abstracts of the papers presented in the plenary sessions and summaries of the recommendations from the Work Groups.

The results set out in these pages exemplify a peculiarly American way of problem-solving: to bring together the informed and the interested, to give each a voice, and to form a consensus which avoids extremes.

We believe that these recommendations are both sound and urgent. If we can learn how to deal humanely with HIV-infected children and to prevent new mothers and children from becoming infected, there is still a chance of stopping the AIDS epidemic. For this purpose, the energies of the American people will need to be mobilized in a "moral equivalent of war" to fight against the spread of HIV.

Stanley A. Plotkin, M.D.
Director, Division of Infectious Diseases
The Children's Hospital of Philadelphia
Professor of Pediatrics and Microbiology
University of Pennsylvania
Professor, The Wistar Institute

EXCERPT FROM KEYNOTE ADDRESS

C. Everett Koop, M.D., D.Sc.
Surgeon General, Public Health Service

Nearly five years ago I came to Philadelphia to stand before a similar group of concerned Americans and share my concerns about handicapped children and their families. My opening remarks at that Surgeon General's Workshop noted that our task would not be easy. We were to consider very complex issues, such as the emotional, the moral, the medical, the technological, the social, the psychological, and the financial issues associated with the care for handicapped children. I also mentioned the awesome challenge of putting a dollar value on a human life.

I wish it were not so, but those remarks are just as appropriate today when we consider yet another problem of major proportion to cope with: the consequences of Human Immunodeficiency Virus (HIV) infection in children and adolescents. Five years ago little was known about the nature and extent of AIDS. And although we suspected that children would become involved, it was then far from reality.

A great deal has changed since that time, as you are well aware. Many of you in this audience have contributed to our expanding knowledge about AIDS or are in some way associated with issues related to this deadly disease. As a result you are familiar with its history. As of the beginning of April 1987, there were among children under 13 years of age 471 reported cases that meet the Centers for Disease Control (CDC) criteria for pediatric AIDS and 139 reported cases among adolescents aged 13 to 19. The nearly 500 cases among young children is *double* the number of cases reported only a year ago. Sixty percent of those children have already died.

Unfortunately, we expect the number of infected children to continue to increase dramatically. By 1991, the Public Health Service estimates that 3,000 children will have suffered from the disease and virtually all will die. As frightening as this may sound, the number is undoubtedly underestimated. We know that HIV infection in children has manifestations that are legion; full-blown CDC-definition AIDS is only part of the story. As many as 2,000 additional children are reported to have symptoms of the infection, but do not fit the specific diagnostic criteria.

It has been found that congenitally acquired HIV infection may affect the infant's central nervous system (CNS) and thus may lead to alterations in growth and development – signs and symptoms not previously identified with AIDS.

With recognition of the wide clinical spectrum of HIV infection in children, the CDC has developed a more detailed and exhaustive classification system for the asymptomatic as well as the symptomatic child, the immunologically compromised child, and the children with neurological disease, lung disease, secondary cancer, cardiopathy, and nephropathy. We know this disease has many presentations in children and, as our knowledge expands, our public health surveillance will continue to reflect this knowledge.

The development of blood-screening procedures and methods of heat treating blood-factor products virtually eliminated the risk of new pediatric AIDS cases from blood and blood products. However, some children had earlier acquired

AIDS from contaminated blood. These children and their families also need our attention. The burden suffered by these children, some of whom may also have a severe chronic illness like hemophilia, is enormous.

About two-thirds of pediatric AIDS cases are the result of transmission from infected mother to child. While there are other modes of transmission of infection to children and adolescents – sexual abuse, drug abuse, and sexual intercourse – our major focus in pediatric AIDS must be on transmission from the infected pregnant woman. Most of these mothers are intravenous drug abusers or sex partners of drug abusers or of bisexual men. As the virus continues its spread among the general population, however, a woman's lack of direct involvement with these high risk behaviors will be no guarantee against her infection and transmission to her fetus.

Present information suggests that up to 65% of babies born to infected mothers will contract the disease. The outlook for these children is almost certain death.

Currently, there are almost no programs that provide coordinated, community-based care for pediatric HIV-infected patients. There is a lack of foster care placement for HIV-infected infants and children. Pediatric units are overwhelmed by the social and medical demands of both ill and well children with HIV infection. There are not enough hospital personnel to provide and coordinate multidisciplinary inpatient, outpatient, community care, and just plain hugging and playing with these children. Pediatric house staff in some institutions where the prevalence of AIDS is high are concerned that their neonatal experience is skewed because of the large numbers of neonates with AIDS.

Many of these children also suffer abandonment by the mother and society. Because of the stigma of AIDS, there are fewer foster homes open to these children. In fact there have been virtually impenetrable barriers between them and a whole variety of social and public health services. Our infants and children with this dread disease must be afforded a normal and dignified life. They must be nurtured, helped to grow and develop, allowed to interact with peers, attend school, and encouraged to enjoy and participate in all activities of childhood, despite a shortened life span.

The AIDS epidemic is imposing severe social and economic burdens on many communities. It will take combined resources from all levels of government and the private sector to meet the increasing costs: of care for an expanding patient population; of educational efforts to reduce high risk behaviors; of maintaining an effective research effort for improved prevention, treatment, and cure; of the social support to juveniles with AIDS and their families to secure the most normal and dignified existence possible.

So far I have been focussing on the issues related to children with AIDS and the heartfelt concern we have for these children. Although we have learned a great deal about AIDS in a short time, our knowledge is nevertheless extremely limited. Prudent judgment must continue to guide us. Under all circumstances we must remain committed to providing humane and dignified care, and we must be willing to bear the responsibilities and costs during the short, troubled lives of these children.

Let us look at this profound tragedy from yet another perspective. Why is there pediatric AIDS? The overwhelming majority of children with congenital AIDS have this disease because of parental prenatal behaviors. While AIDS can afflict children at all levels of society, it is occurring disproportionately in those who have the least capacity and resources to cope. Over half of all babies born with AIDS are black with one or both parents infected with AIDS. Another 25 percent

of all babies born with AIDS are Hispanic.

What we are seeing in reference to AIDS, therefore, is more tragic evidence of high-risk pregnancies and births which are most likely to occur among black women. . . who are poor. . . who are not ready for the world of work. . . who may not even have a high school diploma. . . and who do not have ready access to good prenatal and perinatal health care.

This population of young women produces a disproportionate number of low-birth-weight babies. Life for these babies is a struggle from "day one". . . and many of them never make it to "day two."

This is additional catastrophic news for the black community, already under great economic and social stress. And it's also more evidence of the apparent inability of American society in general to make much headway in helping these young women deal with their own sexuality and their own destinies.

Maternal infection with the HIV is preventable and so too is congenitally acquired AIDS. Assembled here today is a group of national experts from the sciences, the professional community, the government, and the community at-large to address a public health problem of great importance to our nation and to all people of the world. President Reagan has recently called AIDS "Public Health Enemy No. 1." As the Surgeon General of the United States Public Health Service, I am asking you to join with the President to bring all of our skill, expertise, and resolve to focus attention on the broad range of health concerns related to children suffering from AIDS.

Your task for the next several days will be to develop recommendations for a national strategy for reducing the tremendous burden of this devastating condition, especially among our children. I ask that your recommendations give specific attention to the development of an expanded knowledge base, the health resources and services necessary to address the AIDS problem, and the social strategies necessary to assure that our knowledge and resources are best applied in the service of better health for our children.

The recommendations that will emerge from this Surgeon General's Workshop can change attitudes by utilizing calmness, confidence, and clarity in what we say. We must be precise in the use of words lest we exacerbate fear which can only lead to discrimination against children.

In dealing with the specific problems of pediatric AIDS, we need guidelines for our communities to bring together local officials, health professionals, educators, religious leaders, and parents to develop an interdisciplinary, moral, and just approach for the battle against AIDS.

I wish you well and look forward to the fruits of your labors.

You really have the opportunity to make a major contribution to our understanding of pediatric AIDS, and also to the alleviation of some of the burden borne by children with HIV infection and their families.

CITY OF PHILADELPHIA

W. WILSON GOODE
MAYOR

April 6, 1987

CHILDREN WITH HIV INFECTION (AIDS)
AND THEIR FAMILIES WORKSHOP
Philadelphia, PA

TO ALL IN ATTENDANCE:

As Mayor of Philadelphia, I am privileged to extend my best wishes on this most significant workshop, addressing the issue of "Children with HIV Infection (AIDS) and Their Families."

This gathering is a special one, charged with the important task of formulating recommendations to the Surgeon General of the United States, C. Everett Koop, M.D., in helping to set a national policy regarding this growing problem. May all of you in attendance here today be renewed and encouraged in your efforts through the diverse and informative Workshop sessions.

I express my admiration for the commitment and determination of all participants, and I offer my deepest hopes that this workshop will be an unparalleled success in achieving its goals and objectives.

Sincerely,

W. Wilson Goode

W. WILSON GOODE
Mayor

WWG:hs

EXCERPTS FROM PRESENTATIONS

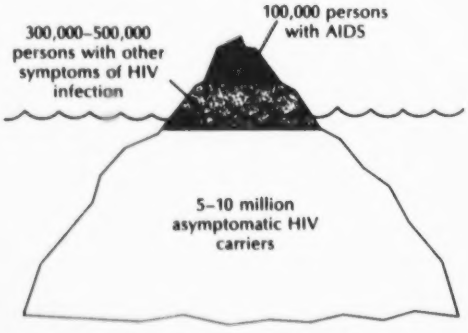
THE GLOBAL EPIDEMIOLOGY OF THE ACQUIRED IMMUNODEFICIENCY SYNDROME

Thomas C. Quinn, M.D.

Introduction

Since its initial recognition in 1981, the acquired immunodeficiency syndrome (AIDS) has become a global pandemic. As of 1 March 1987, nearly 42,000 cases had been reported from over 90 countries. Thirty-two thousand cases have been reported in the United States, an additional 3,000 cases in the other countries of the Americas, 4,500 cases in Europe, and 2,600 cases officially reported in Africa—with several thousand suspected and many more unrecognized in that continent alone. Australia and New Zealand had reported 404 cases for Oceania, and 103 cases had been reported from 10 Asian countries. Because of under-reporting, however, these numbers do not reflect accurately the true incidence of AIDS worldwide. The World Health Organization estimates that there are over 100,000 cases of AIDS throughout the world, with a large majority of these cases occurring in North America and Africa. An additional 300,000–500,000 cases of AIDS-related conditions (ARC) and an estimated 5–10 million people worldwide have already been infected with the virus that causes AIDS, the human immunodeficiency virus (HIV).

Figure 1.


100,000 persons with AIDS
300,000–500,000 persons with other symptoms of HIV infection
5–10 million asymptomatic HIV carriers

This latter group of infected people represents the human reservoir of this infection from which future cases of AIDS will emerge. In the United States, for example, it is estimated that by 1991 over 270,000 cases of AIDS will have developed from the present pool of 1–2 million HIV-infected individuals. In that year, over 54,000 deaths will occur from AIDS, and AIDS will be ranked as one of the leading causes of premature death in our society. For other areas, particularly Central Africa, where already 10%–15% of the general population has been infected by the AIDS virus, these numbers will be even greater. With conservative estimates of 20%–30% of HIV-infected people developing AIDS within a

five year period, and with an 80% mortality rate two years from time of diagnosis of AIDS, AIDS has clearly established itself as one of the most serious epidemics of the century.

AIDS is characterized by the unusual appearance of life-threatening opportunistic infections or malignancies occurring in an individual who has a severe depression of the cell-mediated immune system. Under this clinical case definition, 31,834 patients (including 31,381 adults and 453 children) have been reported as AIDS cases to the CDC as of 2 March 1987. Of these patients, 18,835 (57% of adults and 61% of children) are known to have died, including over 80% of those patients diagnosed before January 1985. Since the initial reports of AIDS in early 1981, the number of cases reported for each 6-month period continues to increase. However, the increases are not exponential, as evidenced by the lengthening period of time required to double the number of cases.

Cases have now been reported from all 50 States, the District of Columbia, and the 4 U.S. territories. Fifty-three percent of all the cases have been reported from New York and California, and the incidence rate of AIDS for New York City and San Francisco is approximately 100 cases/100,000 population.

Adult Patients

Ninety-seven percent of all adult AIDS patients can be placed in a group that suggests the possible means of disease acquisition. Homosexual or bisexual men not known to have used intravenous drugs represent 65% of all reported cases, or 70% of the male cases. Heterosexual IV drug users comprise 17% of all cases, including 15% of the male cases and 51% of the female cases. Homosexual or bisexual men who have used IV drugs comprise 8% of all cases. Persons with hemophilia or coagulation disorders who have received Factor 8 or Factor 9 concentrates represent 1% of all cases. Heterosexual partners of persons with AIDS or at risk for AIDS represent 4% of all cases, including 2% of the males and 27% of the females. The proportion of female AIDS cases in this risk group increased significantly between 1982 and 1986 from 12% to 27%, a trend which may prove to be a good marker for following patterns in heterosexual transmission. This last category of heterosexual partners also includes those who, without other identifiable risk, were born in countries in which heterosexual transmission is believed to play a major role, such as in Haiti and Africa. Recipients of transfused blood or blood components comprise 2% of all cases, which represents 1% of male cases and 10% of the female. For 3% of AIDS patients, the possible means of disease acquisition is undetermined, in these cases primarily due to lack of epidemiologic investigations before death.

Table 1. *Distribution of Etiologic Risk Factors in AIDS Patients in the U.S.A.*

	Male (93%)	*Female (7%)*	*Total*
Homosexual or bisexual men (Non-IVDU)*	70%	–	65%
Homosexual or bisexual men (IVDU)	8%	–	8%
Heterosexual IVDU	15%	51%	17%
Heterosexual partners of persons with AIDS	2%	27%	4%
Coagulation disorders	1%	>1%	1%
Other transfused patients	1%	10%	2%
Undetermined risk factor	3%	11%	3%
	100%	100%	100%

*(IVDU = Intravenous Drug User) (Total 31,381 patients at March 2, 1987)

Pediatric Patients

The percentages displayed in Table 2 have remained fairly constant in the weekly CDC reports. An additional undetermined number of children with evidence of HIV-infection are not included in these numbers because they do not fit the CDC definition for AIDS. These children are defined as having AIDS-related complex (ARC), not a reportable syndrome at this time. Many, if not all, will progress to AIDS.

Table 2. *Demographic and Clinical Distribution of Pediatric AIDS Patients < 13 years)*

AGE:	ETIOLOGIC RISK FACTORS:
(a) < 5 years (88%)	(a) Parent with AIDS or in high-risk category (80%)
(b) > 5 years (12%)	(b) Blood transfusion (12%)
RACE:	(c) Concentrate for coagulation disorders (5%)
(a) Black (57%)	(d) Not known (3%)
(b) Hispanic (22%)	CLINICAL DIAGNOSIS:
(c) White (20%)	(a) Pneumocystis carinii pneumonia (52%)
SEX:	(b) Other opportunistic infection (47%)
(a) Male (55%)	(c) Kaposi's sarcoma (1%)
(b) Female (45%)	

(Total 453 patients at 2 March 1987)

Pediatric patients have been reported from 29 States, the District of Columbia, and Puerto Rico, with 72% of the pediatric patients reported in Florida, New Jersey, and New York. Since the majority of AIDS cases in children are the results of perinatal transmission from the mother, trends in female AIDS cases may also predict future trends for AIDS in children.

Other Countries

The epidemiology of AIDS in other countries of the Americas, such as Canada and Brazil, and in Europe is quite similar to that described for the United States. The male-to-female ratio is 13:1, and there is a predominance of cases occurring among homosexual or bisexual men and intravenous drug users. However, in tropical countries such as in Africa and Haiti, the male-to-female ratio is 1:1 and the majority of cases are identified among heterosexually active individuals who deny the above risk factors. Currently, an accurate assessment of the exact number of cases and risk factors for transmission among those cases is not entirely feasible, due to these developing countries' lack of resources to support an accurate surveillance system. Serologic surveys for HIV infection and preliminary AIDS surveillance studies using modified case definition, however, have provided useful information regarding the spread of HIV infection and AIDS in these areas.

In areas where international scientific teams have been monitoring AIDS, it is estimated that the annual incidence of AIDS is approximately 200 cases/100,000 population, a rate twice that observed presently in New York City or San Francisco. The male-to-female ratio of AIDS cases in Central Africa is approximately 1:1, and the sex and age-specific distribution of AIDS cases reflects patterns seen with other sexually transmitted diseases in which the incidence and morbidity rates are higher among younger women and older men. Serologic studies have indicated prevalence rates of HIV antibody ranging from 5%–88% for blood donors, 27%–88% among female prostitutes, and 2%–10% among pregnant women of Central Africa. Longitudinal data on HIV seroprevalence have shown a rapid rise in HIV antibodies among prostitutes in Kenya from 4% in 1980 to 59% in 1986. These data demonstrate the rapid spread of HIV infection in a high

risk heterosexually active group in Africa. Exposure to infected blood transfusions and blood-contaminated needles used for medicinal purposes further amplify the transmission of HIV among the general population of these tropical areas. Consequently, the entire Central African population has become at risk, and some natural history studies have already documented there a 1% annual seroconversion rate in a general heterosexual population.

As a result of heterosexual transmission, African women of child-bearing age are exposed to HIV. As in U.S. studies, maternal HIV infection appears to be strongly associated with seropositivity among infants in Africa. In one city of Central Africa, approximately 8% of all infants are born to seropositive mothers. While it is unclear what percent of these children will acquire HIV infection perinatally, it is evident that a substantial number of newborn children are presently being infected with HIV. Children in developing countries are also at risk for acquiring HIV infection from unscreened blood transfusions for the anemia associated with malaria, malnutrition, and other endemic diseases, as well as from exposure to blood-contaminated needles and syringes used for medicinal purposes. Thus, it can be anticipated from these data that HIV infection will have a dramatic effect on the general health of these children and potentially on the safety and efficacy of childhood vaccinations.

New Viruses

This problem in Africa is now being exacerbated by the appearance of additional human retroviruses, referred to as HTLV-IV or LAV-2, or HIV-2, some of which may cause symptomatic disease, including AIDS. Infection with these retroviruses is rapidly spreading throughout West Africa, primarily by heterosexual transmission, blood transfusions, exposure to blood contaminated needles and syringes, and perinatally from mother to infant. Diagnostic assays for HIV-2 are not entirely reliable for detection of infection with these other human retroviruses, and new methods need to be developed rapidly to help control the spread of these retroviruses. Additional studies on the relationship of these human retroviruses to HIV, including genomic and protein comparisons, as well as on the pathogenicity and natural history studies, will help facilitate the development of safe and effective vaccines against these human retroviruses.

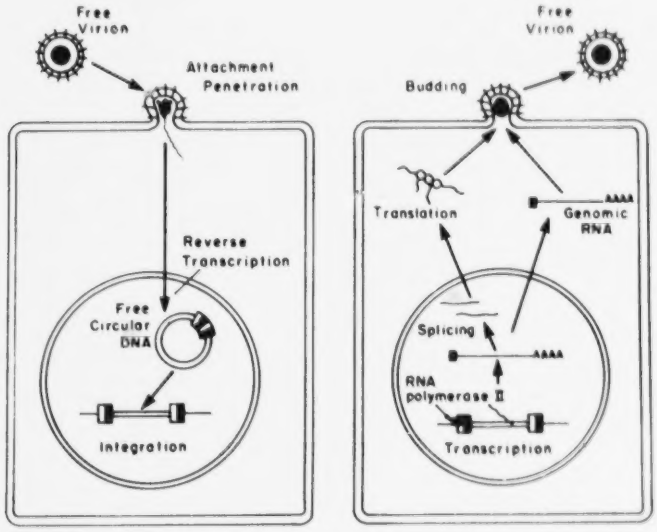
Summary

With an estimated 5–10 million people already infected with HIV, and with projections of 1–2 million cases of AIDS occurring worldwide over the next several years, it is evident that AIDS has clearly become established as a global pandemic, presenting an unprecedented health problem for our society. Unless control efforts are successful, HIV infection will continue to spread rapidly by sexual, parenteral, and perinatal modes of transmission. Until a safe and effective vaccine is available, prevention of HIV transmission must rely primarily on educational programs, modification of sexual practices, screening of blood transfusions, and intensive counseling of seropositive individuals. Faced with one of the greatest epidemics of our lifetime, we must make prevention and control of HIV infection an international public health priority, requiring the full commitment of the necessary political, financial, and professional resources of all countries.

THE HUMAN IMMUNODEFICIENCY VIRUS

Wade Parks, M.D., Ph.D.

The virus etiologically associated with AIDS is a member of the Family Retroviridae. A defining characteristic of this family of viruses is that they have a *diploid* linear single-stranded RNA genome that is surrounded by a protein capsid. The capsid is surrounded by a lipoprotein envelope. This envelope or coat is covered with viral glycoproteins that are involved in viral entry into susceptible cells and is a major target of the host immune system. A unique marker of the Family Retroviridae is the reverse transcriptase which is a part of the virion and which catabolizes the synthesis of DNA from RNA and is thus an RNA-dependent DNA polymerase. The AIDS virus is a member of one of the subfamilies of Retroviridae.



The life cycle of a retrovirus

Figure 1.

The subfamily Lentivirinae that contains the AIDS retrovirus includes a number of unglulate viruses associated with chronic, persistent infections in their natural hosts. These include Equine Infectious Anemia (EIA) or "swamp fever" described first in 1904, Visna – the prototypic lentivirus which causes a neurologic disease of sheep, and Caprine Arthritis and Encephalitis Virus (CAEV). The morphology of lentivirus virions is relatively unique with an elongated, bar-shaped nucleoid. Lentiviruses have a slightly larger genome than most retroviruses, and a larger and more highly variable virion external glycoprotein than other retroviruses. Thus far, the reverse transcriptase differs only slightly, preferring a different divalent cation – magnesium – over manganese.

The etiologic agent of AIDS was originally termed the Lymphadenopathy-Associated Virus or LAV by Luc Montagnier and his co-workers at the Institut Pasteur in Paris. When Robert Gallo and his colleagues at the National Cancer Institute repeatedly isolated virus from AIDS patients, they referred to their isolates as Human T-Lymphotropic Virus type III, or HTLV-III. Gallo and his group had already described an HTLV-I and HTLV-II, human-infecting members of the Family Retroviridae, subfamily oncovirinae. Hence, the etiologic agent of AIDS was called HTLV-III in this country and LAV in Europe and frequently abbreviated HTLV-III/LAV. More recently, a group of virologists have recommended the term, Human Immunodeficiency Virus (HIV), for the AIDS virus.

The retrovirus of AIDS has a structure that is similar to other retroviruses. This means that the linearized form can be depicted as bound on either end by two non-coding regions known as long terminal repeats (LTRs). Moving 5′ to 3′, the gene order is *gag*, *pol*, and *env* between the LTRs. The *gag* gene encodes for structural proteins of the virus, including the p24 molecule, which is the most abundant polypeptide of the virion and which is very important as a diagnostic marker in infected patients. The *pol* gene encodes for the reverse transcriptase, a remarkable polyfunctional molecule which subserves proteolytic, catalytic, and integration activities within newly infected cells. The *env* gene encodes for the virion surface proteins, which are glycosylated, hence glycoproteins. The transmembrane protein is known as p41E and is the major component of newer recombinant diagnostic seroassays for detecting infection. The external glycoprotein is known as gp120. The gp120 contains the region that forms the attachment to the viral target, the CD4 molecule that characterizes certain T-lymphocytes. This high affinity ligand interaction is the mechanism by which the virus can infect cells. Antibodies to the gp120 can neutralize viral infectivity. The gp120 has multiple regions that are highly variable in genetic sequence; these regions differ from one virus to another. Thus, the virus varies markedly, enabling the virus to avoid elimination by the host's immune system.

Finally, the AIDS retrovirus has some additional genetic features that demonstrate its amazing versatility. Within the virus there are a number of open reading frames that have the capacity to encode for proteins. Two of these have been described: *tat* and *art*. Both are products of spliced mRNAs and appear to subserve important biological roles for viral replication. The *tat* gene especially codes for a protein that binds to a very specific region of the 3-LTR and then enhances transcription. Since the protein can act in trans, it is called the trans activator (tat). The *tat* gene product serves to turbocharge the replication of the AIDS retroviruses. Hence, in the short time that an infected lymphocyte may undergo cell division in response to a given antigenic stimulus, *tat* and its related proteins allow maximal production of the retrovirus and thereby increase the probability for successful virus infection of other lymphocytes.

In general, the retrovirus of AIDS is a highly adapted pathogen. Its genetic functions subserve two essential prerequisites for any virus's survival, replication and avoiding immune elimination. A full knowledge of the molecular mechanisms of viral replication and their relevance may be central to the control of the AIDS epidemic.

THE IMMUNOLOGY OF PEDIATRIC AIDS

Arthur J. Ammann, M.D.

The pathogenesis of AIDS, felt to be a result of HIV infection, is best studied in infants and children, since they represent a more pristine host. Undoubtedly, HIV infection and its resultant clinical manifestations are a consequence of infection with this retrovirus as well as the interaction between HIV and other preexisting or subsequent infectious agents. Studies of infants suggest that HIV infection alone may result in impairment of the immune system and secondary susceptibility to opportunistic infection. Even in the case of isolated HIV infection, however, the clinical manifestations and severity of the disease may vary, implying that the time at which infection occurs (as early as 20 weeks gestation), the amount of viral inoculum, and preexisting immunodeficiency are important variables.

Experimental evidence suggests that the monocyte/macrophage may be the initial cell infected with HIV and may subsequently be a major source of continued virus replication and infection. It is important to emphasize that certain organs have significant numbers of monocytes and macrophages that are CD4 receptor-positive (the CD4 receptor is required for HIV infection of cells). This may provide an explanation for the occurrence of the isolated brain and lung involvement sometimes observed in infants with HIV infection. In vitro infection of monocytes with HIV may result in giant cell formation, with a histologic appearance similar to that of the giant cells found in tissue sections obtained from the lung and brain of HIV-infected patients.

The interaction of HIV and other viruses may result in clinical features unique to either adult AIDS or pediatric AIDS. For example, Kaposi's sarcoma—a frequent malignancy in AIDS—has not been convincingly demonstrated in pediatric AIDS. On the other hand, chronic parotid swelling and pulmonary lymphoid interstitial pneumonitis (LIP) are frequently found in pediatric AIDS but rarely observed in adult AIDS.

The pathogenesis of LIP was linked to infection with Epstein-Barr virus (EBV) in several studies which used EBV DNA probes to detect the presence of virus in lung tissue. The response to EBV infection in patients with AIDS is abnormal. In EBV-infected infants with AIDS followed prospectively, virus was cultured for several weeks prior to appearance of antibody to EBV antigen. There was an absence of an IgM anti-VCA response and failure to develop antibody to Epstein-Barr Nuclear Antigen (EBNA). IgG antibody to Anti-Viral Capsid Antigen (VCA) and antibody to Early Antigen (EA) remained high in most patients, suggesting persistent chronic EBV infection. This is in contrast to normal individuals where infection results in an initial increase in antibody to VCA, followed by a decline to low levels which persist for life.

Patients with pediatric AIDS and EBV infection also have prolonged virocytemia, easily recoverable EBV, and increased numbers of EBV-infected cells. It is possible that the existence of HIV infection in the lung, followed by EBV infection, results in a lymphoid proliferative response manifested as LIP. EBV-infected B cells are more susceptible to HIV infection than uninfected B cells and may be stimulated by HIV antigens to excessive proliferation. A suggested interaction between HIV and EBV was based on observations in EBV-

infected adults who subsequently became infected with HIV and developed additional immunologic abnormalities. The more common sequence of infection in pediatric AIDS, HIV followed by EBV infection, may result in a lymphoproliferative disorder. Adults have a reverse sequence more commonly, and they rarely develop LIP.

The presence of LIP may modify the susceptibility of infants to opportunistic infection. Two studies note that patients with LIP had fewer opportunistic pulmonary infections and that patients with Pneumocystis carinii pneumonia (PCP) do not have evidence of pulmonary hyperplasia.

HIV infection of immunocompetent cells may result in immunodeficiency by several mechanisms. Following infection, syncytia formation and fusion of cells occur with subsequent death in vitro. A similar mechanism in vivo could result in T-cell depletion. Cytotoxic T-cells may also destroy infected cells in vivo resulting in reduced numbers of T4 cells and the characteristic reversed T4/T8 ratios seen in most patients. However, early immunologic abnormalities occur prior to depletion of immunocompetent cells, suggesting that HIV infection may directly interfere with immune function. For example, HIV infection of T-cells in vitro results in decreased IL-2 and CD4 receptor mRNA and IL-2 and CD4 receptor expression. It is also known that Peripheral Blood Mononuclear Cells (PBMC) from patients with AIDS and preAIDS have decreased cytokine production in vitro. Many of these cytokines are essential for immune interaction, antiviral, and antitumor effects. Deficiencies of interferon-α (IFN-α), interferon-γ (IFN-γ), tumor necrosis factor-α (TNF-α), tumor necrosis factor β (TNF-β), interleukin-2 (IL-2), and interleukin-1 (IL-1) have been described. One or more cytokine deficiencies may result in secondary defects, such as abnormal monocyte/macrophage function, decreased natural killer-cell activity, decreased antibody formation, and decreased T-cell immunity.

Abnormalities of macrophage function may play a more critical role in the pathogenesis of HIV-induced immunodeficiency than previously appreciated. The macrophage may act both as a reservoir of HIV infection and, as a result of its central role in the T- and B-cell immunity, may play a primary role in early immunodeficiency.

Immunodeficiency following HIV infection may also result from the immunosuppressive effects of HIV envelope glycoprotein or other immunosuppressive regions of virus proteins. Following HIV infection, envelope glycoproteins are secreted to the surface of cells. Several regions of the envelope glycoprotein are capable of suppressing the immune response in vitro. Glycoprotein 120 (gp120) is capable of binding to the CD4a region of the CD4 receptor and interferes with immune function in vitro as measured by mitogenic and antigenic stimulation.

Prospective studies of patients with AIDS suggest that B-cell abnormalities may precede other laboratory features of immunodeficiency. Patients usually have polyclonal hypergammaglobulinemia. This may result from chronic HIV antigen stimulation or loss of suppressor T-cell regulation. In contrast, antibody levels to HIV antigens are not markedly elevated as is usually observed in other chronic viral infections. Further, specific IgM antibody to HIV is difficult to demonstrate in either acute or chronic infection. As the syndrome progresses, patients lose their ability to respond to other antigens following immunization.

Table 1. *B-Cell Abnormalities in AIDS*

- Polyclonal hypergammaglobulinemia
- Failure to produce antibody following immunization
- Increased spontaneous IgG secretion, due to:
  1) antigenic stimulation by HIV
  2) increased numbers of EBV infected cells
  3) HIV-induced T-cell dependent B-cell activation
- Decreased B-cell response to antigens
- Decreased B-cell response to T-cell independent mitogens

T-cell abnormalities are numerous and profound. Early abnormalities consist of inability of PBMC to respond to antigens in vitro and of cytotoxic T-cells to kill target cells. In vivo, this correlates with absence of reaction to delayed hypersensitivity skin tests. As the syndrome progresses, PBMC from patients lose their ability to respond to mitogens and alloantigens and are unable to produce normal amounts of essential cytokines (IFN-α, IFN-γ, TNF-α, TNF-β, IL-1, IL-2). The broad-based T-cell deficiencies are most likely a result of both intrinsic abnormalities and severe T-cell depletion.

Table 2. *T-Cell Abnormalities in AIDS*

Number
- Lymphopenia
- Decreased T helper cells (decreased H/S ratio)
- Decreased T suppressor cells
- Increased Dr and OKT10 expression on CD8 cells

Function
- Absent delayed hypersensitivity skin tests
- Diminished PBMC response to antigens
- Diminished PBMC response to mitigens (PWM, Con A, PHA)
- Decreased cytokine production
  IL-1, IL-2
  IFN-α, IFN-γ
  TNF-α, TNF-β
- Decreased Thymic hormones (thymulin)

A number of monocyte defects have been reported in AIDS. Monocytes fail to mature at a normal rate, do not have normal chemotaxis and adherence, and, as determined by use of certain in vitro assays, are unable to kill some microorganisms. An unanswered critical question is whether antigen processing or antigen presentation of HIV-infected macrophages is abnormal.

The major abnormality of the complement pathway which has been described in AIDS is that of increased immune complex formation. This is probably a result of both non-specific polyclonal hypergammaglobulinemia and chronic antigenemia as a consequence of chronic infection with a number of microbial agents. Some of the severe consequences of chronic immune complex formation, such as renal failure, are rarely observed in patients with AIDS. However thrombocytopenia, which is more commonly found, may result from removal of immune complex coated platelets from the circulation.

Table 3. *Complement Abnormalities in AIDS*

- Increased circulating immune complexes
- Increased HIV specific immune complexes
- Immune complex deposition (renal disease, thrombocytopenia)

In order to establish a diagnosis of HIV infection, either antibody to HIV or the presence of HIV must be demonstrated. A number of tests for antibody are commercially available. Most of these are enzyme-linked immunosorbent assays (ELISA) and utilize HIV antigens coated on to plastic surfaces to detect IgG antibody in the test serum. The assays are designed to be highly sensitive and therefore readily detect antibody positives, but as a consequence also have a high rate of false positives.

Table 4. *Enzyme Linked Immunosorbent Assay (ELISA)*

- Method
  1) Disrupted virus placed in plastic wells or on plastic beads
  2) Incubated with test serum
  3) Antibody to antigen detected by enzymatic reaction.
- Characteristics
  1) Sensitive - best for screening
  2) High number of false positives
     (< 50% are confirmed positive by Western blot)
  3) A positive must be confirmed by Western blot

It is necessary to confirm each positive by first repeating the ELISA and then, if again positive, confirming the presence of antibody to specific HIV antigens by a Western blot. Other antibody assays include indirect immunofluorescence and radioimmunoprecipitate assays and are primarily for investigational purposes.

A major difficulty in the diagnosis of HIV infection in newborns and infants is the inability to differentiate between passively transferred maternal IgG antibody to HIV and actively produced antibody from the infant. Unfortunately IgM antibody to HIV has been detected only inconsistently. There are several other methods of establishing HIV infection in the infant. Serial antibody testing by Western blot may demonstrate the emergence of new antibodies to HIV antigen. Culture of PBMC for virus or the use of DNA probes may demonstrate presence of HIV, but the methods are currently less sensitive than antibody assays. Newly developed assays for the detection of HIV antigen in serum may provide an alternative means of testing.

A diagnosis in pediatric AIDS can be confirmed using a few well established assays of immunologic function coupled with assays for virus infection or demonstration of viral antigen. The confirmation of HIV infection is essential to provide appropriate care for infected infants and children.

TRANSMISSION OF HUMAN IMMUNODEFICIENCY VIRUS INFECTION IN THE UNITED STATES

Martha F. Rogers, M.D.

The human immunodeficiency virus (HIV) is transmitted by three routes: 1) from mothers to infants during the perinatal period, 2) through parenteral exposure to infected body fluids, primarily blood, and 3) through sexual contact. Although other modes of transmission have been proposed, including transmission through casual contact, through insect bites, through exposure to contaminated needles used for tatooing, ear piercing, or acupuncture, and through receipt of hepatitis-B vaccine or immune globulin, there is little or no evidence supporting such occurrence.

Perinatal Transmission

Perinatal transmission accounts nationwide for about three-quarters of cases of HIV infection in prepubertal children. The epidemiologic characteristics of these children closely parallel those of heterosexual adults with AIDS, particularly women. Over half (65%) of reported cases of AIDS in women, 69% of heterosexual men with AIDs, and 73% of the perinatally acquired AIDS cases in children were related to IV drug abuse or sexual contact with IV drug abusers. The geographic areas most affected by heterosexual and perinatal transmission have been the New York City metropolitan area, northern New Jersey, and southern Florida. The majority of heterosexual men (74%), women (72%), and children with perinatally acquired infection (88%) have been black or Hispanic. Most are inner-city dwellers of low socioeconomic status.

Evidence suggests that perinatal transmission can occur by three modes: 1) transplacental passage of the virus in utero, 2) exposure to infected maternal blood and vaginal fluids during the labor and delivery of the infant, and 3) post partum ingestion of breast milk containing the virus. The proportion of perinatally acquired cases attributable to each of these modes is unknown.

Preliminary data from prospective studies of infected women and their infants indicate that the frequency of transmission from mothers to their infants may be as high as 50%. Both symptomatic and asymptomatic women can transmit HIV to their infants. The risk factors associated with transmission, however, have not been defined. Mothers can transmit HIV in more than one pregnancy. Each infected infant is at risk of developing AIDS.

Table 1. *Possible Risk Factors for Transmission of HIV from Mothers to Their Infants*

Viral factors – viremia, latent vs. active infection, % cells infected
Substance abuse or other environmental/behavioral factors
Other infections present
Level of immune suppression
Continued exposure to HIV
Host factors

These prospective studies also indicate that maternal HIV infection is probably not associated with adverse prenatal or neonatal infant outcomes, nor with an increase in obstetrical complications. Two studies have reported an increased frequency of spontaneous abortions among seropositive women, but three other studies have not observed this trend. To date none of the women in the CDC Classification-3 or less developed AIDS during the pregnancy. In one study, however, a trend towards an increased incidence of hospitalizations for infections in seropositive versus seronegative pregnant women was observed. In addition, a greater proportion of seropositive pregnant women developed complications during an average of 6 months' follow-up postpartum, compared with seropositive women who did not become pregnant and who were followed an average of 12 months.

Parenteral Transmission

Transmission through parenteral exposure to infective body fluids has occurred primarily in 2 populations: 1) in persons sharing contaminated needles used to inject illicit drugs, and 2) from donors to recipients of blood or blood products. Transmission through accidental injuries with contaminated needles or other cutting objects in the health care setting has been extremely rare, occurring in less than 1% of such injuries.

About one-fifth of reported AIDS cases are attributable to transmission through use of contaminated needles for injecting illicit drugs. Seventy-four percent of these patients come from New York and New Jersey. Seroprevalence studies of IV drug abusers have shown infection rates of up to 70% in these areas, 42% in Boston, 11% in Chicago, and 10% in San Francisco. Several studies have shown that in IV drug abusers, seroprevalence is highest in those who are black or Hispanic.

Transmission through receipt of infected blood or blood products accounts for 3% of adult and 17% of the pediatric AIDS patients nationwide. Cases are scattered throughout the United States with California and New York having the greatest number of cases. Most of the children with transfusion-acquired AIDS were transfused in the neonatal period or had coagulation disorders.

No cases of transfusion-acquired AIDS have been reported in children transfused after initiation of donor screening for HIV antibody in March–April 1985. Although transmission through transfusion of seronegative blood can occur when the donor is in the early stages of HIV infection and is viremic but not yet producing antibody, this has been rare.

In one study of the recipients of blood collected prior to HIV screening from donors who later developed AIDS, the risk of HIV infection following receipt of blood from an infected donor approached 100%. In instances of split donations, in which one recipient became infected, so did the other. Once a seropositive donor transmitted the virus to a recipient, all subsequent recipients of blood from that donor also became infected.

Although donor screening procedures and heat treatment of coagulation products have markedly reduced the transmission of HIV through these routes, cases of AIDS in persons who received these products before these interventions will continue to occur. The incubation period for AIDS in adults with transfusion-acquired infection averages 3 years and has been as long as 7 years. The incubation is shorter for children, averaging 2 years and ranging up to 6 years.

Sexual Transmission

Sexual contact is the most common mode of HIV transmission in adults, and accounts for over three-quarters of reported cases. Sexual contact between homosexual or bisexual men has accounted for 95% of sexually acquired HIV infection, but heterosexual transmission is increasing, particularly in minority populations. In contrast to gay male cases, about three-quarters of women with AIDS and of heterosexual men with AIDS are black or Hispanic.

The frequency of transmission between heterosexual sex partners is around 10%–15% in the partners of hemophiliac men and transfusion recipients, about 40% in the non-drug-abusing partners of IV drug abusers, and about 58% in a study of partners of primarily IV drug abusers and Haitian immigrants. Some persons have acquired infection after only a few at-risk sexual encounters, while others did not acquire infection despite repeated contact over several years. Medical conditions (such as cervicitis or vaginitis), menstruation, and sexual practices (anal intercourse) that involve greater exposure to blood and friable tissues increase the likelihood of transmission. Transmission has occurred, however, in persons engaging in vaginal intercourse exclusively and without any of the above conditions.

Casual Contact

Transmission through close but nonsexual contact (so called "casual") has been extremely rare. Only three possible cases have been reported. Two of these cases involved nursing care of bedridden patients associated with extensive and repeated contact with blood and body fluids of the infected patient. The other case involved apparent transmission between two siblings, but the nature of the contact was not well characterized. Nine other independent studies of over 400 family members of HIV-infected patients have not found evidence of household transmission. In addition, none of the family members of the over 30,000 AIDS cases reported to the Centers for Disease Control (CDC) has developed AIDS as a result of household contact.

Intervention methods designed to prevent further spread of HIV infection must consider the epidemiology of the infection including the modes of transmission, the characteristics of the currently affected populations, and the potential for spread within these populations and to other groups.

APPROACHES TO PREVENTION OF HIV INFECTION

Walter R. Dowdle, Ph.D.

The five basic mechanisms for prevention of infectious diseases include 1) immunoprophylaxis (vaccine), 2) chemoprophylaxis/therapy (drugs), 3) sanitation (environment), 4) lifestyle modification (behavior), and 5) vector control. Of these five mechanisms, the first four are applicable to prevention of HIV infection. There is no evidence to suggest that the AIDS virus is transmitted through insect or other vectors.

The first two of the four mechanisms, vaccines and prophylactic/therapeutic drugs, are under development. Ideally, both will be incorporated into future strategies. Much progress has been made toward understanding the basic properties of potential retrovirus vaccines, but 5 to 10 years or more may be required before a vaccine can be realistically considered as a public health tool. How a vaccine will be utilized in prevention strategy will depend upon its availability, cost, efficacy, and safety. Greater promise has been shown for antiviral drugs, particularly as we learn more about the pharmacology and clinical efficacy of certain classes of drugs.

For the present, however, our strategy must rely on the two remaining mechanisms, modifying the environment and modifying personal behavior.

Modifying the environment is of limited benefit, but some changes have already been accomplished. Tests for screening the blood of donors for HIV antibody have been used regularly for nearly two years. This screening has vastly reduced the risk of transfusion-associated infections. Donor screening and treatment of factor VIII has virtually eliminated the risk of AIDS for persons with hemophilia. The environment does not pose a major risk for health care workers. Needlestick injury would appear to be the greatest concern, but recommendations for caution by health care workers have been widely disseminated. Our main task has been to reassure the public that the general environment does not present a threat. The virus is not transmitted through casual social contact or food and water.

The remaining and most important mechanism for prevention consists of modifying behavior. This is a difficult and often controversial task that in the past has not been considered effective for other sexually transmitted diseases (STDs). Nevertheless, we must make a concerted effort to develop effective educational programs regarding HIV infection. Specific mechanisms for modifying behavior include modification of sexual practices of infected persons, routinely offering testing and counseling to persons at high risk, treating IV drug abusers to preclude transmission of the virus through the use of contaminated needles, and information and education programs. There is considerable evidence that risk reduction already has occurred in the gay community.

Effective information/education programs include a whole spectrum of activities, ranging from TV spots to individual counseling sessions. An effective program requires multiple channels of information tailored to specific audiences and delivered through the auspices of a wide range of private and public organizations and institutions. The Public Health Service Information/Education Program is directed to the general public, to school- and college-aged young persons, to other persons at increased risk, and to health workers. The program is budgeted

at over 79 million dollars, with 102 million proposed for next year. The general public can be informed and educated through hotlines, coalitions, ad campaigns, and clearinghouses. That, of course, forms the foundation and background on which more specific programs aimed at high-risk groups can be developed. Each of the nation's school systems will decide how best to implement education in AIDS prevention at appropriate ages. There is less argument here than may appear on the surface. Our interest is in assisting local school groups in developing their own curricula. We are trying to facilitate that activity, but by no means is the Federal government attempting to tell anyone what to teach. The individual school boards will make their own decisions. We do feel that there is great demand and eagerness in the schools to move on the education issue.

Efforts at educating health workers can be productive, because they are a major channel of information to infected patients and in carrying preventive information to others.

When we speak of educating those at increased risk for pediatric AIDS, the preferable strategy is to prevent infection in women of child-bearing age. This is a very difficult area. Those at increased risk are the female sex partners of men at high risk, intravenous drug users, prostitutes and clients. These are difficult to reach. The second line of defense is to provide counseling to those already infected to help them enter into a program of comprehensive health care and follow-up, including avoidance of pregnancy. After that, our options grow less and less clear.

In some geographic areas and for some populations, these information/education activities are beginning. To ensure maximum effectiveness, these programs must be constantly evaluated and modified if necessary. Increased knowledge and general awareness of prevention information is important, but our ultimate criterion of success must be a change in personal behavior that results in decreased transmission of infection.

NATURAL HISTORY OF HIV INFECTION IN CHILDREN

Gwendolyn B. Scott, M.D.

One hundred thirty-four cases of perinatal Human Immunodeficiency Virus (HIV) infection were identified in South Florida between January 1981 and December 1986. Each year since 1981, we've seen an increasing number of cases. In 1986 we identified one-third of our total case load, and so far in 1987 we are seeing at least one new case per week. These infants were born to 109 infected women. Drug abuse accounted for 22% of the disease in the mothers in comparison to 60% reported nationally. Fifty-one of these children meet the CDC surveillance criteria for AIDS; 81 others have clinical symptomatology and are diagnosed as ARC. Two, who are now 7 years old, are asymptomatic.

Ninety-two percent of these children were black. The majority of children presented with clinical disease in the first two years of life (74%). There are, however, a number of children who present between the ages of 2 and 6 with the first manifestations of disease. The overall mortality in these children is 35%, but among those who meet the criteria for AIDS, the mortality is 73.5%.

Pneumocystis carinii pneumonitis (PCP) and Candida esophagitis are the most common opportunistic infections. Failure to thrive is the presenting complaint. Lymphadenopathy, hepatosplenomegaly, and persistent oral thrush are some of the more common findings. We have seen disseminated cytomegalic virus infection frequently, five cases of cryptosporidiosis, and one case of Mycobacterium avium-intracellulare. Tumors occur, but are rare in children. We have a few cases of Kaposi's sarcoma, one of lymphoma of the liver, and one of Burkitt's lymphoma of the lung. Opportunistic infections presenting in the first year of life are associated with a higher mortality.

In an effort to better describe the clinical outcome of infection in pediatric cases, a syndrome approach has been applied.

Table 1. *Syndromes Associated with Pediatric HIV Infection*

Wasting Syndrome
Lymphoid Interstitial Pneumonitis
Recurrent Bacterial Infection
Encephalopathy
Lymphadenopathy Syndrome
Cardiomyopathy
Hepatitis
Renal Disease

More than one of these syndromes may occur in the same patient separately or simultaneously. There appears to be a relationship between the immune response and the development of these syndromes. For example, patients with early onset pneumocystis pneumonitis or encephalopathy tend to have decreased evidence of immune response and have a higher mortality. In comparison, patients with LIP, lymphadenopathy syndrome, cardiomyopathy, recurrent bacterial infections, or renal disease generally have a lymphoproliferative response with hyper-

gammaglobulinemia, lymphadenopathy, and hepatosplenomegaly. Children with PCP have an earlier age of onset and a higher mortality rate than those with LIP.

Table 2. *LIP and Early Onset PCP*

	LIP	PCP
Mean Age of Onset	15.8 mos.	6.2 mos.
Median Age of Onset	13.5 mos.	5 mos.
Overall Mortality	25.7%	85.7%

The overall mortality for PCP is 85.7% as compared to 25.7% in the LIP group. The immune response in these groups differs. PCP is associated with a lymphoablative response, while LIP is associated with a lymphoproliferative response. A greater understanding of the spectrum of disease and knowledge of the natural history of the various syndromes will allow better predictions of prognosis. Although not all HIV infected children die early in life, this is an illness that is unpredictable and is associated with a high rate of morbidity and mortality.

The child is usually the first member of the family that is identified as being infected. In this situation, screening of the parents and siblings is indicated. In the majority of cases, the mother is asymptomatic at the time of diagnosis of HIV infection in her infant. Of the 109 mothers in our patient population, 30% have subsequently developed AIDS or ARC. Seventeen mothers have died.

This series of patients has offered us the opportunity to evaluate the risk of an HIV infected pregnant woman delivering an infected infant. Twenty-three HIV infected women have had 40 subsequent infants after the birth of the index case. Not every subsequent infant will be infected. We have followed one woman who has delivered four infected infants, but another mother had an infected infant and subsequently delivered three uninfected children. Still another had an infected infant, an uninfected one, and then another infected one. We obviously do not know what factors cause a mother to pass the infection on to her infant. Of all the subsequent infants, 52% are infected. This represents a substantial risk for these women and emphasizes the importance of identifying them so they can receive appropriate counselling regarding pregnancy. This population may represent a special population of women, and further studies are underway to determine the risk of having an infected child in an HIV-positive woman who has not had previously infected infants.

In conclusion, pediatric HIV infection presents with a broad spectrum of disease and is associated with a high mortality rate. The majority of children with this disease are black or Hispanic and reside in the lower socioeconomic areas of the inner city. It is important to recognize infected children early so that appropriate instructions for care can be given to the parent and regular medical followup can be instituted. In addition, with the development of anti-viral drugs, early diagnosis and recognition will be imperative, so that early treatment can be given. Screening of the family is important to identify infected family members and to give appropriate counselling and education. The HIV-positive woman is at risk for giving birth to an infected infant. Prevention of perinatal infection will only be accomplished by prevention of disease in women or by other interventions, such as drug therapy. Identification of HIV-positive women is important so that appropriate education and counselling can be provided.

NATURAL HISTORY OF HIV INFECTION II

James Oleske, M.D.

Estimates from the CDC suggest that by 1991 there will be 12.5 million Americans infected with the AIDS virus (Human Immunodeficiency Virus – HIV) and 250,000 of these will be symptomatic AIDS cases. Based on our experience and those of others caring for pediatric AIDS cases, by 1991 there may be 10,000 to 20,000 symptomatic HIV infected infants and children in the USA.

Our difficulties in providing care to over 60 active pediatric AIDS cases at Children's Hospital of New Jersey in Newark indicate major problems in the near future. The health care requirements of infants and children infected with HIV are extensive and include the complex tertiary medical capabilities of a pediatric hospital and intense psychological services. The care we provide to these children includes vigorous nutritional support, including placement when necessary of intravenous catheters, early hospitalization for treatment of possible infection episodes, and monthly replacement therapy with intravenous gamma globulin. Tissue biopsy of lung, lymph nodes, thymus and bone marrow, as well as CAT scan, gallium scan and esophagoscopy are frequent requirements in the clinical evaluation of these children. Research and time consuming investigational drug studies are now being undertaken on our patients. All of these activities – diagnosis, clinical care, and necessary research – have placed an enormous burden on the available resources at our children's hospital. Besides the medical dilemma posed by AIDS, there is the significant public misunderstanding of this disease with ongoing stigmatization of patients and their families.

The development of antibody screening tests has substantially reduced (although not eliminated) the risk of blood transfusion acquired AIDS. It is true that the majority of cases of AIDS in children is due to perinatal exposure from an infected mother, but for the next five to six years we must follow a cohort of newborns who received small blood transfusions in the nursery between 1980 and 1985, and who are at risk of developing this disease. As pediatricians we must insist that we have safe blood products for use in children and that we use blood products appropriately.

It doesn't take a sophisticated laboratory to make a diagnosis of AIDS. If the epidemiology and the clinical historic patterns are present, we are comfortable in Newark making the diagnosis after simple laboratory studies including: Complete Blood Count (CBC), quantitative immunoglobulin assays, liver function testing, chest X-rays, and HIV antibody testing. Anemia leads the list of abnormalities. These children are almost all anemic and most have elevated liver enzymes.

Table 1. *Laboratory Findings in Infants and Children*

Hypergammaglobulinemia/Hypogammaglobulinemia	Anemia
Depressed T-helper cells	Leukopenia
Reversed lymphocyte subset ratio	Thrombocytopenia
Depressed lymphocyte responses to mitogens	Elevated level of circulating immune complexes
Decreased specific antibody responses	Elevated serum transaminase levels

The clinical spectrum of illness in children with HIV infection is expanding as our experience with this disease increases. When we looked carefully at our

AIDS and ARC children with failure to thrive, we realized that many of these infants had problems with the central nervous system. Many had a chronic encephalopathy. Others had primary HIV infections of the CNS, with failure to thrive and loss of developmental milestones, the equivalent of the dementia seen in adults. A child who is otherwise well can present with primary CNS infection without any other manifestation of AIDS, and even an essentially normal immune system.

Table 2. *Neurologic Findings in Children with HIV Infection*

Developmental Delay/Loss of Developmental Milestones	Motor Dysfunction
Chronic Encephalopathy	Microcephaly
Seizure Disorders	Abnormal CT Scan Findings – Cortical Atrophy, Calcifications

One of the clinical problems we have had is dealing with the gastrointestinal manifestations. These children have a variety of GI problems including distension, diarrhea, inability to eat, and tremendous discomfort. The resultant effect is marked malnutrition. In seven of fifteen autopsies, we saw cardiovascular abnormalities. Three were congestive cardiomyopathies and four arteriopathies. One case resulted in a fatal coronary artery aneurysm.

Unlike adults, infants with HIV infection will most likely be symptomatic over the course of their illness. There are some differences between pediatric and adult AIDS, and these are outlined in the following table.

Table 3. *Differences between Pediatric and Adult AIDS*

1. Kaposi's sarcoma and B cell lymphoma are rare in children
2. Hepatitis B infection is less frequent than in adults
3. Hypergammaglobulinemia is more pronounced in children
4. Peripheral lymphopenia is uncommon in children
5. Lymphoid interstitial pneumonitis (LIP) is much more common in children
6. Some children will have normal ratio of helper to suppressor T cells (although quantitatively T helper cells are diminished)
7. Serious bacterial sepsis is a major problem in children
8. Dysmorphic features may be found in some children
9. Acute mononucleosis-like presentation is rare in children
10. Progressive neurologic disease secondary to primary HIV CNS infection is more pronounced in children

The final mortality rate is unknown, but with our present program at Children's Hospital, we have seen the mortality rate decrease to 35%. With the use of intravenous gamma globulin therapy, the quality of life for our patients has improved, with recurrent septic episodes decreasing from 45% in 1983 to 5% in 1986. We try to provide optimum care to each child, comprehensive rehabilitation services, early intervention programs, and psychological support for the families of our patients. We have learned that HIV probably causes primary infections not only of the immune system, but also of the CNS, heart, kidneys, and liver. This primary multisystem/organ infection with the HIV virus as well as its known secondary opportunistic infections and malignancies present a major problem in devising therapeutic programs. Educational programs regarding the real risk of transmission, i.e., blood contaminated needles used in drug addiction, and sexual contact, need to be extended to school age children and hard-to-reach risk populations. If child-bearing age women at high risk for HIV infection would avoid pregnancy, we eventually would see no new cases of pediatric AIDS.

HIV TRANSMITTED BY BLOOD PRODUCTS

Margaret W. Hilgartner, M.D.

The extent to which the national blood supply has been contaminated by the Human Immunodeficiency Virus is unknown. With a basis of epidemiologic data, however, one can say that the virus probably came into the blood supply in 1977. Retrospective study of stored samples of hemophiliac plasma showed the appearance of anti-HIV antibodies in 1979 in a few patients (i.e., became seropositive) and in the majority of hemophiliacs during the years 1980–1983. The first hemophiliac was reported with the disease in 1981. When widespread testing of the donor population became available in March 1985, 0.4%–0.9% of donors were found seropositive nationwide, with the highest figures in those cities (New York, Miami, Los Angeles, and San Francisco) with the greatest reported number of AIDS patients.

Incidence

The CDC has recorded a total of 939 cases of AIDS related to transfusions of HIV-contaminated blood products as of 2 March 1987. This figure is 2.9% of the total persons reported with AIDS and includes all adults, adolescents, and children. Of this total, 287 individuals have had hemophilia or other coagulation disorders and have been transfused with fresh frozen plasma, cryoprecipitates for factor concentrate, while 652 individuals have been transfused with red blood cells or components of blood.

When the figures for the children are separated from the total, we find that 78 children or 18% of the total 453 children reported with AIDS have had the virus transmitted via blood and blood products. Of those, 24 (5%) have had hemophilia and 54 (or 12%) have been transfused for other reasons. Although these numbers are increasing with time, the percentages of the total have remained stable. The higher percentage in babies transfused with blood or components is probably related to the shorter incubation period seen in infants, while the percentage in young hemophiliacs is only slightly higher than the figures seen in the adult hemophiliac.

Natural History

Information about the natural history of the disease in the transfused patient is evolving slowly, but with some accuracy, because the date of transmission of the infected blood can be ascertained in many cases. A wide spectrum of disease seems to exist, with variables related to age, underlying diseases for which the transfusion was given, and the product used for transfusion. The Red Cross "Look Back" study currently going on in all Blood Banks is tracing recipients of blood from donors known to have been HIV-negative on subsequent testing. The Transfusion Safety Study (TSS) is enrolling all donors and recipients of HIV-positive blood donated in the six months prior to universal screening of all donors for seropositivity in four high risk cities in the United States. With these two studies, one hopes that complete epidemiological information will be obtained concerning the natural history of AIDS as transmitted through blood products. At present, data from the TSS show that 90% of those patients who received a

unit of blood found retrospectively to be HIV seropositive have themselves become seropositive. Although 75% of recipients died within one year after the transfusion of causes not related to AIDS, there is a potential reservoir of unsuspecting anti-HIV positive individuals deserving close follow-up and counseling.

Children tranfused in the newborn period who subsequently developed AIDS were first reported in 1983 by Ammann et al., who found that symptoms appeared six months to three years post transfusion. Others have shown that the incubation period from transfusion to the appearance of symptoms seems shorter in those children who were transfused as very small premature babies, when compared to the older child where the incubation period may be the same as in the transfused adult. In the adult, Curran has shown that the incubation period may be 15 months to 57 months (mean 27 months), and current CDC data suggest a span of seven years. In addition, Curran showed that blood components other than those used by hemophiliacs could transmit AIDS.

The product used for transfusion has marked influence on the transmission of disease. Those products containing white cells appear to have transmitted disease more readily than red cell products. For example a set of twins seen at The New York Hospital were transfused with components from the same donor. The twin receiving the red cells did not become HIV positive, while the twin receiving the platelets developed signs and symptoms of AIDS within 16 months.

Those who received a greater number of transfusions in the period 1980–1985 are more likely to be seropositive than those receiving a smaller number of transfusions or single donor units. For example: only 12% of the 84 transfusion-dependent thalassemia patients at The New York Hospital-Cornell Medical Center in New York City are seropositive. The figures for hemophiliacs, however, are as follows:

Table 1. *HIV Status of Hemophiliacs – NYH/CUMC*

Total Anti-HIV Positive		119/163	73%
Adults	≥ 18 years	83/94	88%
Children	< 13 years	19/43	44%
	< 18 years	36/69	52%

The thalassemia patients have a donor exposure of 12–24 per year, while the hemophiliac may have a donor exposure of 800,000 to 1 million per year. The single donor unit is less likely to be contaminated than the pooled donor product from which the factor concentrates for the hemophiliac are manufactured.

The hemophilia patient population, however, appears to be different from the homosexual or IV-drug-using population in relation to progression of HIV disease and infectivity of sexual partners. For example: only 20%–30% of the seropositive hemophiliacs have the syndrome of AIDS related complex (ARC), and only 2% have developed symptoms of AIDS. This figure appears substantially lower than for the homosexual population, where 30%–35% of those followed longitudinally have developed AIDS.

Measures Taken to Prevent Transmission of HIV in Blood Products:

Although HIV transmission via blood transfusions was recognized before a test was available to define the HIV antibody status, decisive measures could not be designed to insure the purity of the national blood supply. In the spring of 1984, the New York Blood Center developed a confidential intake questionnaire allowing

the center to determine whether the donor was at risk and thereby to designate whether the blood donation should be used for transfusion or discarded. This process of self-exclusion allowed the donor to preserve his confidentiality and contribute to improving the quality of the blood supply. Self-exclusion has now been adopted by all other blood collection agencies.

Table 2. *Measures Taken to Prevent Transmission of HIV in Blood and Blood Products*

1. Self-elimination of at risk donors
2. Screening of Donor – March 1985
   HIV antibody testing (ELISA)
3. Treatment of pooled products:
   Heat-wet or dry state
   Solvent/Detergent
   B-Propriolactone, U-V Light
   Monoclonal antibody derived
   Recombinant DNA derived
4. HIV – Antigen tests

Treatment of the pooled plasma concentrates of clotting factors was begun in 1984 to decrease the amount of hepatitis virus contamination. Subsequently all of the methods used were found effective in the elimination of HIV: Beta propriolactone, ultra-violet light, solvent-detergent treatment, and heat have been used to treat the concentrates in the wet or dried state. The Dry Heat method is the current choice. Monoclonal antibody separation and recombinant manufacture of factors are being tested and appear promising.

In 1985 the ELISA screening tests were introduced to identify blood or plasmaphoresis products containing HIV-positive antibodies. These tests are 99.2% specific for antibody and 93.4%–99.6% sensitive. The Western blot test performed on all positive donations is 75% sensitive for HIV antibodies. Newer ELISA tests currently being tested are even more specific than those in use. With all of these tests, the blood supply has been rendered virtually free of donations contaminated with HIV.

The problem remains for the donation given in that period between infection and development of antibody. A few recipients of red blood cells from units which tested seronegative at time of donation have become antibody positive; the blood donor has also subsequently become antibody positive. Many more are being identified with the "Look Back" program. We look forward therefore to the licensure and marketing of a test for HIV antigen which will close the time span between infection and antibody development, so that we may have a national blood supply completely free of HIV.

SUPPORTIVE CARE AND TREATMENT OF PEDIATRIC AIDS

Arye Rubinstein, M.D.

This summary addresses some specific issues which may alter the course of the disease.

Supportive Care

Failure to thrive due to a variety of etiologies is one of the major features of pediatric AIDS. In some cases, malabsorption and protein-losing enteropathy are identified. In others, it may be related to factors such as chronic infection. Proper nutritional support (adequate caloric and protein intake) in many instances may be crucial for the care of the child with AIDS. Where this goal cannot be achieved by oral feedings, one has to consider nasogastric feeding or intravenous hyperalimentation. In our experience nasogastric feeding is of limited value. Generally, weight gain could be achieved through intravenous hyperalimentation using venous (broviac) access, but this may be compromised by the development of infections in the access lines.

Infection Control and Prophylaxis

Probably the most frequent problems in children with HIV infection, especially under the age of 2 years, are recurrent bacterial infections which may progress to sepsis and meningitis. The optimal strategies to prevent these infections have not yet been established: I) Antibiotics (trimethoprim-sulfa, ampicillin). Several groups have suggested that the use of prophylactic antibiotics may avert the catastrophic outcome of acute infections, especially in those patients who have a severe underlying B cell deficiency. The drawbacks for the use of prophylactic antibiotics are the development of side effects, resistant bacterial strains, and poor compliance. II) Intravenous gamma globulin. Intravenous gamma globulin has been applied in pediatric AIDS since 1981. The rationale for the use of this therapy was the documentation of an underlying B cell defect. In our experience this approach has significantly reduced bacterial infections, especially in the younger age group. Many unresolved issues exist with regard to this treatment: 1) what dose is to be used; 2) is the higher dose currently used by us (300mg/kg) advantageous over the low dose used in some agammaglobulinemic patients (100–200mg/kg) with regard to a) the delay of immunological attrition, b) prevention of infections, and c) removal of circulating immune complexes; 3) although no risks have been involved with intravenous gamma globulin, it is a costly treatment and requires a twice monthly 2–3 hour hospital short-stay admission; 4) should the European double-blind control study on IV gamma globulin be duplicated in the U.S.; and 5) should gamma globulin be used in any HIV infected child who has a B-cell defect or should it be restricted to those who present clinically with infections.

Treatment of Specific Infections

Certain infections in AIDS are extremely difficult to manage.

Our experience demonstrates that salmonellosis is extremely hard to eradicate. Trimethoprim-sulfa, ampicillin, or ceftriaxone have failed in many cases to elim-

inate the carrier state. While in immunocompetent hosts the carrier state is of no risk, children with AIDS who are carriers of salmonella often suffer recurrent septic episodes. New strategies should be designed, therefore, to treat this condition. One of the promising medications is Fluroquinolone used at 400mg twice a day.

Pneumocystis carinii pneumonia (PCP). The most frequently utilized treatment includes trimethoprim-sulfamethoxazol. In cases of failure, pentamidine is introduced. Other medications such as dapsone in combination with other treatments or as an alternate treatment have not shown great promise.

Disseminated cytomegalovirus (CMV) infection with/without retinitis. No treatment has achieved permanent improvement. Trisodium phosphonoformate (Foscarnet) may have a role.

Varicella. A benign disease in immunocompetent children, varicella may be life-threatening for immunocompromised patients. Children with apparently normal in vitro lymphocyte mitogenic responses to specific and non-specific mitogens and with normal T4 cell numbers and percentages have developed fatal varicella. We, therefore, have adopted the policy of administering acyclovir in any case where an extensive vesiculation occurs or where new vesicles develop after the fourth day of the disease.

Treatment Modalities for the Direct or Indirect Control of HIV Infection

1) Immuno-reconstitution or immuno-potentiation. A whole host of such modalities has been attempted in adults, including: bone-marrow transplantation, thymic transplantation, thymic hormones, alpha and beta interferon, interleukin-2, intravenous gamma globulin, isoprinosine, imuthiol, and enkephalins. The results have been disappointing. They do not appear to control the virus, and some of these immunopotentiating agents may activate virus replication. Experience with these agents in children is limited. Several thymic transplants have been performed but did not result in permanent objective benefit. The use of thymic transplants and thymic hormones in children is of special interest, since children with HIV infection demonstrate early in the disease course low levels of thymulin (FTS). Our trials with thymic hormone – fraction V – have not yielded encouraging results. Thymic hormones seem to temporarily improve T cell functions, but subsequently a phase of rapid immunological attrition and disappearance of T4 cells was detected.

2) Antiviral agents. A number of antiviral agents have been used in adults. These include reverse transcriptase inhibitors such as ansamycin, suramin, Foscarnet, AZT, dCT, AL-721, a lipid component that promotes the extraction of cholesterol from the viral membrane, and ribavirin (Virazole) which inhibits guanyl transferase in the capping of the 5' end of HIV mRNA. Currently the two most promising drugs are AZT and dCT. Phase I trials with AZT in children with AIDS are in progress. In adults it has major side effects. dCT seems to have less side effects in adults, but has the disadvantage of limited penetration of the blood-brain barrier. The frequent and devastating CNS disease in children with HIV infection has to be taken into consideration when an antiviral agent is selected. Infection of fetal brain could be documented in the first trimester of pregnancy. Brain atrophy can also be documented in neonates by CT scans. Consequently, early treatment of CNS disease is imperative. Any antiviral drug that does not penetrate the blood-brain barrier, therefore, may be of little benefit for the treatment of HIV infection in the pediatric age group.

3) Hyperimmune Serum. We have used hyperimmune serum intravenously since May 1984. Its benefit for the control of HIV infection has not yet been established. Hyperimmune serum, however, may have a major role in the prevention of infection. It should be considered for use in HIV-infected women during early pregnancy to prevent fetal infection.

4) Combination treatments. Two forms of combination treatments are to be considered: a) the combination of various antiviral agents. Some in vitro studies suggest, however, that the combination of two or more antiviral agents may result in antagonism. For example, in vitro AZT and ribavirin seem to antagonize each other's effect on the AIDS virus; and b) the combination of antiviral agents and immunopotentiation. Antiviral agents may avert the activation of HIV by immunopotentiating agents.

INTRAVENOUS DRUG ABUSE AND WOMEN'S MEDICAL ISSUES

Constance B. Wofsy, M.D.

Epidemiology

Women constitute 7% of all reported AIDS cases in the United States, in striking contrast to the ratios elsewhere. Of women with AIDS, 28% are white, 51% are black, 20% are Hispanic/Latino.

Table 1. *Women with AIDS*
Percent of Total AIDS Cases

	International
Central Africa	40%–50%
Haiti	20%–25%
Canada, France	12%
U.S.*	7%

*If male homosexuals/bisexuals and hemophiliacs are excluded, women make up 30%

Fifty-two percent of women with AIDS are intravenous drug users (IVDUs), but 27% are non-IVDUs who were infected by a male sexual partner, usually an IVDU male. Of importance, 78% of women with AIDS are between the ages of 13 and 39, the peak childbearing ages. In pediatric AIDS, 45% of white and 88% of non-white children acquired the disease from an IVDU parent.

It is estimated that there are more than a half million regular or casual IVDU women in the United States. As many as 75,000 women IVDUs and 20,000 non-IVDU female partners of male IVDUs may already be infected with the virus. With an estimated 1–2 million Americans infected, there may be 200,000 women who carry the virus. Many haven't a clue that they are infected. The most highly represented populations of infected women, IVDUs and nonwhites, are already highly stigmatized, but we must not let fear of stigma immobilize educational efforts.

Transmission

HIV has been isolated from blood, semen, and cervical secretions. Transmission can occur by vaginal intercourse from man to woman and from woman to man. Long-term sexual partners having unprotected sex with an infected person for several years have a 15%–45% chance of becoming infected. An interesting study done in Miami examined the percent of seroconversion in 32 couples after they learned that one was seropositive. Eight chose abstinence and none seroconverted. Ten chose to use condoms and only one seroconverted. Fourteen did nothing in the way of protection and 12 became seropositive.

Table 2. *Relationship Between Condom Use and Seroconversion*

	N	SEROCONV	%
Abstinence	8	0	0
Condom	10	1	10
No Condom	14	12	86

Fischl, et al. *JAMA* 1987; 257:640.

Sexual partners who also share needles are at even greater risk.

Women Who Use IV Drugs

IVDUs are hard to reach. Only an estimated 15% are in treatment programs. To reach others, we must rely on community networks, health clinics, jails, schools, churches, and the media. For those with little education and short attention span, the message must be simple and direct, and the language culturally specific. Many who use drugs do not perceive of themselves as users. Those who do not understand the health risks and the need to clean needles may continue to share because they erroneously consider their partner to be nonrisk. Sharing is socially expected; the urgency of the fix exceeds the risk; carrying drug paraphernalia like a clean needle or bleach bottle may make one subject to arrest. The sexual and needle risks for the woman often come from a man who is also a user, and even more recalcitrant in acknowledging his own risk and in taking responsibility for his female partner.

Our research group in San Francisco studied 289 sexually active women, none of them prostitutes, and found that 5% were seropositive. These were self-referred, so they do not represent a cross-section of the city. All of the seropositives have a personal history of intravenous drug use or have a sustained relationship with a specific high-risk partner. For over a year and a half, we followed 200 women with no such personal history and found only one seroconversion in a city rampant with HIV.

Women IVDUs have few resources. They often have responsibility for children, multiple health problems, lack of family support, lack of money, depression, and low self-esteem. Prostitution may be a means of support for the drug habit and family.

HIV Infection and Pregnancy

IV drug use does not inhibit fertility; some of these women have several children and may desire more. Birth control is often limited because of perceived lack of risk of pregnancy, irregular periods, decreased sexual frequency as a result of drug use, and lack of power to control the sexual expectations and preferences of male partners.

Few programs are targeted at pregnant addicts. Existing programs may be costly and too understaffed to deal with family patterns of abusive treatment, implementation of childbearing skills, and birth control education.

An infected woman has a 20%–60% chance of passing infection to her child. An infected child is very likely to die, or be severely ill by two years of age. Pregnancy may accelerate HIV expression in the woman and thus should be avoided for the sake of mother and child. In one study, however, it was found that 25% of infected babies were born to mothers who hadn't a clue they were infected or that their partners were in a risk group. The infected infant established the mother's diagnosis.

Many women who have had an infected child nevertheless have proceeded to have additional children despite intensive culturally specific counseling. Childbirth may provide self-esteem or be culturally expected.

Clinical Expression of HIV Infection in Women

The spectrum of HIV-related infections and malignancies is similar in men and women, except that women rarely get Kaposi's sarcoma. Gynecologic problems do not seem to be significantly increased.

Symptoms of HIV infection in women may be overlooked by physicians for

many reasons. Non-IVDU women are perceived to be a low risk group and HIV symptoms are nonspecific. IV drug users have medical problems whose symptoms mimic HIV related disorders (e.g., bacterial endocarditis, cotton lung, skin infections). Physicians may feel inadequate to the task of AIDS care, may wrongly assume that all infected women are IV drug users or prostitutes, or may not have overcome their own fears. It is known that strong stigma and profound repercussions may result from the identification of an infected individual. Availability for HIV testing or adequacy of the medical staff and community to deal with the consequences are lacking. Thus, strong clues to infection may be overlooked and women may proceed under the illusion that there are no risks.

Societal Issues for Women Infected with HIV

HIV infected women come from all walks of life. Forty-eight percent don't use IV drugs. Many issues cross all class, race, and cultural boundaries—for example: 1) extreme isolation—infection is often kept rigorously secret, depriving women of the desperately needed support of family, friends, community, and particularly other infected women; 2) profound grief for the loss of health, body image, sexuality, and childbearing potential; 3) unavailability of medical care, counseling, child care, housing, and related services; 4) lack of informed primary care, OB/GYN, sex counselors, and abortion counselors; 5) the burden of making decisions about initiation, continuation, and termination of pregnancy; 6) the lack of natural "community," such as shared by gay men; 7) the abruptness of the diagnosis, which may be disclosed at the birth of an infected baby or death of a spouse; 8) loss of self-esteem—feeling dirty, useless, unwanted, and unlovable; 9) the feeling of responsibility from watching a child die; 10) the stigma that "women with AIDS are prostitutes who infect their children"; and 11) lack of male responsibility, and the societal assumption that women have the responsibility for control of sex and conception.

Importance of all Women to the AIDS Epidemic

Women still constitute the large bulk of the country's educators and caregivers through roles of teachers, nurses, social workers, counselors, girlfriends, wives, and mothers. All persons in these positions shoulder a great responsibility. They are expected to overcome their own fears, become comfortable with sexual, drug, and lifestyle issues, acquire wisdom, nurture and teach the young, comfort the fearful, and care for the sick. It's a tall order.

EDUCATION TO PREVENT HIV INFECTION

Karolynn Siegel, Ph.D.

Education regarding modes of transmission of HIV infection remains the most important public health strategy for controlling the spread of AIDS. Education must mean more than just imparting information about practices that place one at risk of becoming infected or of infecting others. It must also aim: to motivate or persuade people to adopt certain behaviors and relinquish others, to eliminate irrational fears about transmission through casual contact, to debunk myths and stereotypes about the "kind of people" who get sexually transmitted diseases, to dispute notions of culpability or blame for the epidemic, to instruct all levels of society in safe sexual practices, and to insure cooperation in anti-drug programs.

While there is widespread agreement on the central role that education must play in stemming the epidemic, there is somewhat less agreement on who should be educated and at what ages, what messages should be communicated, and who should assume responsibility for this education. These issues are currently the focus of much public discussion and debate.

I want to emphasize the need to create a collective sense of national purpose in combatting this disease. AIDS is still viewed by the majority of people as the problem of a few select and socially isolated groups. We must strive to overcome a "we/they" mentality. We must promote a feeling that as a society we all have a shared interest in controlling this epidemic, which must take precedence over more narrow self or special group interests. Everyone needs to feel a personal investment in bringing about a solution to the problems the epidemic has posed.

The establishment of a national office of AIDS education, or a national director of AIDS education, as recommended in the Institute of Medicine report, would constitute a very important first step. The public must receive a clear and unequivocal message that this problem merits a national plan of action and concerns all Americans.

In England, Prime Minister Thatcher recently distributed a flyer under her name to every household in the country, informing people of the seriousness of the AIDS problem and telling them what they could do to protect themselves. This action sends a clear and powerful message to the populace. It says that this matter has the attention of the highest leaders of the country; every citizen should be informed about it and concerned with helping control it.

I would like to move on to the question of "who should be educated?" Clearly, we must continue to focus heavily on the established risk groups – gay and bisexual men and intravenous drug users and their partners.

We must target extensive educational activities to blacks and Hispanics, groups greatly over-represented among those with AIDS. We must enlist ongoing cooperation of support groups, community leaders and community-based organizations and must always consider cultural norms. We must find a way to tie the hoped-for behavior change into their own value and belief system. The importance of bearing a healthy child may be used to help persuade women to use condoms as protection against AIDS and other sexually transmitted diseases (STDs).

We know that adolescence is a time of experimentation that often involves drug use and sexual experimentation. The AIDS epidemic has increased the urgency to reach a goal of having "every junior and senior high school student receive timely STD education."

A principal concern is how we should communicate. Here, we can draw some lessons from our efforts over the past few years to educate risk groups members – especially gay men. Our own research indicates that some of the messages contained in risk-reduction guidelines, which have been used as a principal educational tool among gay men, have sometimes had unintended negative consequences. Recommendations like "know your partner" and "reduce your number of partners" have often created a false sense of security. One can rarely take the kind of exhaustive sexual history from a prospective partner that would be necessary even to begin to evaluate the degree of risk inherent in sexual encounter. We have found that men who continue to engage in risky sex, but with fewer partners or nonanonymous partners, believe that they have adequately reduced their risk of infection because they are in compliance with safe-sexual-practices guidelines. Similar messages are being used now in educational materials directed to the heterosexual public.

While multiple messages about different prophylactic behaviors may not seem to be competing with each other, they are. The message we communicate should be unambiguous, confrontational, and consistent. There are only two acceptable adaptations to the threat of the infection – abstinence, or using a condom in every sexual encounter where a risk of transmission may exist. If you offer people several alternative ways to adapt, they will usually choose the course of action that involves least personal change. There would be no problem if the alternatives were all equally efficacious, but they rarely are.

Who should do the educating? The source of any message is an important determinant of the attention it will receive. Therefore, I would recommend that we make greater use of opinion leaders in trying to alter the public's attitudes toward the epidemic and modify sexual norms among sexually active individuals. Opinion leaders are widely esteemed public figures who have the confidence and trust of much of the public. Because they are respected and trusted, their positions on matters are sought and afforded a special consideration. They can perform an especially valuable role in shaping public attitudes around such controversial issues as AIDS.

There is the need to develop strategies for changing social attitudes and norms to support the adoption of behavior that will slow or halt the spread of infection. Social norms can be a powerful force in constraining certain practices. The need for the acceptance and approval of others is an important motive in shaping behavior. Peer social pressure is the most compelling force for modification of life style of adolescents in particular.

Sex has always been considered a private act. Now, however, we are compelled to recognize that it can sometimes have public consequences. We can no longer afford to assert the position that what someone else does sexually is solely his own business. We must acknowledge that we have a vested interest in employing positive social sanctions to encourage people to conduct themselves in a way that will contribute to the control of the epidemic. We have to create a social environment in which abstinence is a positively sanctioned option. For those individuals who choose to engage in intimate sexual relations, we must confer social approval

on those who behave in a sexually responsible way. People must come to regard the use of condoms as a normative expectation.

At this time, we must depend on the schools to educate children about AIDS, STDs, and drug use. To pretend that we can rely on parents is really to abrogate our responsibility and to know this may leave many children unprepared to protect themselves against these threats.

There are no easy answers to the problem of educating the public about AIDS. While there is some base of knowledge and experience to guide us, the difficulties that confront us are formidable. For example, the popular perception that AIDS remains a "medical mystery" and that there is disagreement even among the supposed experts on some matters greatly complicates the educational task. When available scientific evidence is regarded as indeterminant or provisional, its power to influence behavior is likely to be significantly diminished.

LEGAL ISSUES SURROUNDING MEDICAL CARE, TREATMENT, AND RESEARCH OF CHILDREN

Harold Ginzburg, M.D., J.D., M.P.H.

Introduction

The ethical and legal issues surrounding informed consent and the individual right of privacy in the care and treatment of minors and in their participation in research protocols thus far are not unique to those infected with HIV. We can apply precedents derived from previous decisions. These form a base from which to build ethical and legal criteria to manage issues created by the AIDS epidemic, some of which may now be unforeseeable.

The Right to Knowledge: Informed Consent

Informed consent is a merger of the sharing of knowledge and the receipt of permission to proceed with the therapeutic or research intervention; informed consent is educated consent. Obtaining such consent from a competent adult is significantly different from obtaining consent for a minor or incompetent adult. A clinician or clinical investigator should seek informed consent only under circumstances that provide the prospective patient or research subject or their respective legal representatives with sufficient opportunity to consider whether or not to participate in the treatment or research. The decision-making process should be free of the possibility of coercion or undue influence. The information provided by the health care professional must be in language that the patient or research subject can be expected to understand. No informed consent, either oral or written, may include any exculpatory language through which the subject or representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability or negligence.

Informed consent has become a structured and formal process; a written document is prepared by the medical institution which explains the proposed medical treatment or medical research. The basic legal tenet of modern informed consent is over 70 years old. Justice Cardozo stated that:

> "Every human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient's consent commits an assault and battery for which he is liable in damages... [A person] is considered to be master of his own body, and he may, if he be of sound mind, expressly prohibit the performance of life-saving surgery or other medical treatment.... The law does not promote [a physician] to substitute his own judgement for that of the patient."

The American Hospital Association (AHA) has promulgated "A Patient's Bill of Rights" which states in part: "The patient has the right to receive from his physician information necessary to give informed consent prior to the start of any procedure and/or treatment" and "The patient has the right to be advised if the hospital proposes to engage in or perform human experimentation affecting his care or treatment. The patient has the right to refuse to participate in such research projects." Another policy statement of the AHA deals with collaborative (physi-

cian and patient or research subject) decision-making as the basis for informed consent. The need for essential information to be present in the language familiar to the *patient* (or his parent or guardian) and the need for formal documentation of the presentation of such information have resulted in lengthy informed consent forms that are specific to the condition being treated. Gone are the "blanket" informed consent forms hospitals have used in the past.

The medical and legal (professional) communities have long held that neonates and young children are not able to give meaningful consent for medical care and treatment. Parents are presumed to be in the best position to speak the mind of the child under the substituted judgment theory. Thus, parents or court-appointed legal guardians may give legally binding permission for children to receive medical treatments and also to become participants in research protocols. Few would argue about the appropriateness of the parent or guardian being the responsible person for authorizing medical treatment for their child or ward. Enrolling a child in a medical research protocol, however, is a more complex issue. Although the potential benefits of participation in research protocols (extended life or an improved quality of life) may often be substantial, many of these research protocols also may present substantial risks to the child. What are the decision-making processes that will maximize the potential benefits of medical science to the non-consenting child while protecting his or her fundamental rights?

The Right to Privacy

The right to privacy is a fundamental constitutional right; this right may be overridden only by the demonstration of a compelling State interest. While minors are legally presumed not to be able to give informed consent or withhold consent for their medical care and treatment [in most jurisdictions this is an "irrebuttable" presumption (i.e., it cannot be successfully challenged in a court of law)], the *parens patriae* doctrine, the doctrine of informed consent in emergencies, the "Infant Doe" regulations of the United States Department of Health and Human Services, and numerous cases where a court-appointed guardianship is created to permit the treatment of a minor over the objections of the parent(s) (e.g., Jehovah's Witness' blood transfusion cases)—all support the general presumption that medical care and treatment should be provided to minors. Adults do have a right to refuse treatment, even if it will lead to their demise; they do not have the right to extend their personal beliefs to their children when the outcome of such an imposition is irreversible.

The minor's personal right of privacy has been invoked when the guardians or parents, after determining that the minor is terminally ill and medical care offers no real hope of restoring health, have declined treatment. Historically, refusing necessary and life-saving treatment has constituted child abuse. In such circumstances the court may intervene, in *parens patriae*, to act as the general guardian, granting consent for the initiation of medical treatment. The court generally will not intervene in this role to grant consent for the initiation of an experimental medical treatment.

The final regulations of the Department of Health and Human Services to implement the Child Abuse Amendments of 1984 to the Child Abuse Prevention and Treatment Act, 42 USC section 5101(a), enacted October 9, 1984, indicate that medical neglect (failure to provide adequate medical care) and withholding of medically indicated treatment, in the medical care of infants, are to be based on "reasonable medical judgment" and not on "quality of life standards." The final

rule requires that procedures be developed consistent with State law to obtain access to medical records and/or other pertinent information when such access is necessary to assure an appropriate investigation or a report of medical neglect.

The Judicial Council of the American Medical Association states that the decision whether to exert maximal efforts to sustain life should be the choice of the parents in consultation with the treating physician. Parental authority should be respected unless there is convincing evidence to the contrary. There is a substantive consensus on the deliberate withholding of life-saving treatment:

1) The law will support a decision not to provide treatment that would be futile or inhumane; no available treatment or surgical procedure offers any hope of survival; heroic efforts would be invasive, traumatic, and painful; medical opinion on diagnosis and prognosis is clear and unanimous.
2) The law will support terminating life-support for a patient whose brain has irreversibly ceased to function.
3) The law will defer, in matters of honest professional disagreement, to well-reasoned medical-ethical decisions which are the result of free and open communication among all concerned parties.

The tension develops when, as in HIV infections, there is no acute decision to be made; the clinical course, though predictable, is not rapid; and the quantity of pain and suffering cannot be estimated, with any degree of medical certainty, before it occurs.

The Duty to Warn

Individuals with HIV antibodies have a right to medical confidentiality, but is it the physician's duty to warn those in foreseeable danger of contracting HIV from an infected individual? When, and under what circumstances should individual liberties, such as medical confidentiality, be abridged for the good of the community? If the female partner has not been notified that her male consort is seropositive or infected, becomes pregnant and delivers an infected child, is there liability? And for whom? The physician? The male consort? Both? These and other questions, basic to the medical care of children with a variety of health conditions, become all the more difficult when the condition is HIV infection.

MANAGEMENT OF THE CHILD WITH HIV INFECTION: IMPLICATIONS FOR SERVICE DELIVERY

Mary G. Boland, R.N., M.S.N., C.P.N.P.

Management of the Child with HIV Infection: Impact on Health Care Services

In areas where HIV infection is epidemic, children with HIV infection and their families are straining the resources of health care delivery systems and human services agencies. The child and family have multiple medical, social, and emotional needs. The need for children to receive day care and attend school is forcing communities to deal with AIDS-related issues at the local level.

While a small number of children acquire the disease as a result of transfusion of infected blood and blood products, the majority of infected children acquire AIDS perinatally. Mothers of these children are infected, and it is not unusual for both parents and one or more siblings to be infected and ill. Thus, the parents are confronted by issues regarding their own health status as well as that of the child. For the most part, children who get this disease and their parents are disenfranchised. They are not like the gay community, which is able to mobilize itself. They need health care providers who are not only sensitive to their needs but knowledgeable regarding the disease, and willing to advocate for the children and their families.

About 80% of the children come from a home where one or both parents have a history of drug abuse. Because of problems related to drug use, many families are already receiving assistance from multiple health and human service agencies. The majority of the families are headed by a single parent, usually the mother, who is eligible for or receiving public assistance and Medicaid. After the diagnosis, many of the children are eligible for and do receive Supplemental Security Income (SSI) and Medicaid. Prior to the diagnosis, 25% of the families in our program were known to the child protective services agency (Division of Youth and Family Services), and many were already in foster care. For most children, placement occurred because of unwillingness or inability of the mother to care for the child, rather than as a result of illness in the child. Active intravenous drug use resulted in inability of the mother to provide food and shelter for the child. In two families, acute encephalopathic symptoms in the mother required legal action and placement of the infant with other family members. We have no boarder babies in our institution and have a good record in terms of identifying foster homes for our children when we have needed them.

Initially, many of the mothers appeared well. However, as length of follow-up has increased, more mothers are becoming symptomatic, and several have died. Progressive physical illness in the mother decreases the energy available for care of the child. Impending death of a caretaking parent prompts discussions regarding long term care of the child. While grandparents and other extended family members frequently accept care of the child, they are dealing with grief due to loss of the parent and justified fears regarding the death of the child whose care they assume. In one family where both parents and one of two infected children have died, the maternal grandmother gave home care for the mother and child, and is now caring for the surviving infected child and his well siblings.

The existence of both progressive and static encephalopathy has been described in children with HIV infection. Of the 61 children in our program who underwent comprehensive developmental evaluations, only 5% tested at an appropriate age level in all areas. Delays occurred predominantly in speech and language development and acquisition of motor skills. A few children actually lost achieved milestones. Parents, however, rarely identified developmental delays as an area of concern. It is not a population of people who come in saying, "I think my child is behind; he is not walking; he is not talking." We often find it difficult to get the message across that there are developmental delays to address in terms of their child's later education. For instance, we have no child in a handicapped preschool program at this point. Parents are afraid to enroll their children because they hope things will get better and because they are afraid of what will happen to the older sibling when the diagnosis becomes known in the community.

In the infant and child, HIV infection can produce dysfunction of various organ systems requiring care by multiple pediatric subspecialists. Institutions such as children's hospitals that provide tertiary level care are best suited to provide the range of services these children require. To date, the New Jersey Children's Hospital AIDS Program (CHAP) has provided on-going care for 89 children from 81 families. In most families, the child is the index case and identification of other infected family members occurs after diagnosis of the child. While the goal of treatment programs is to maintain the child within the home and community, there are occasions when hospitalization is necessary.

We have an outpatient visit about once or twice a month per child, the majority for intravenous gamma globulin therapy. Our average of hospitalizations is between 2 and 3 a year per child, with a range of 0–7. The majority of admissions are for pulmonary disease, either Pneumocystis or complications related to lymphoid interstitial pneumonitis. After that, septic-like episodes and otitis predominate.

The morbidity and mortality resulting from HIV infection demands an approach to care that is comprehensive and coordinates care between the hospital, home, and community. The ill child must be viewed as a member of a family system that, however weakened or malfunctioning, has its own tasks and stages that are disrupted by illness in the family members. HIV infection is a life threatening but chronic process that has the potential to destroy an entire family.

We have developed a child-centered, but family-focussed, program to treat the illness and its symptoms while attempting to prevent further disruption of the family unit. We have adopted many of the concepts related to the chronic childhood illness model, because much of it applies to children with AIDS. Despite the pessimistic statistics, they are living longer. We have several children in our program who were infected from birth, sick as infants, and are now school age and in school. Our oldest perinatally infected child is eight.

Figure 1.

The need to collect epidemiological data, the multiple health and developmental problems resulting from infection, and the implementation of drug treatment trials as more antiviral agents become available – all require that programs regionalize services to cover a contiguous but wide geographical area. These programs must be multidisciplinary and utilize physicians, nurses, nutritionists, social workers, and developmental specialists.

Health care providers in the acute setting must be willing to reach out and form innovative partnerships with the various agencies providing service to these children and their families. These types of model programs can provide direct services, including collaborative case management with agencies in the child's community.

Table 1. *Children's Hospital AIDS Program*

Nursing Services
- Coordination of Care and Service
- Ongoing Assessment of Parental Health and Coping Ability
- Identification of Resources
- Collaboration with Other Disciplines
- Advocacy in the Health Care Setting and Community

Social Services
- Assessment of Family System
- Ongoing Counseling for Child and Family
- Support Groups for Families
- Assistance to Families in Navigating the Bureaucracy of Social Agencies
- Collaboration with Other Disciplines

In addition, the expertise of program staff can be utilized to provide outreach education to health care providers, as well as to advocate for the child and family within the community.

CURRENT DEVELOPMENTS AND FUTURE PROSPECTS FOR AIDS VACCINES

Gerald V. Quinnan, Jr., M.D.

Prevention of infection from human immunodeficiency virus (HIV) is dependent on avoidance of exposure and the successful application of measures which prevent transmission. The availability of a safe and effective vaccine would be an extremely valuable adjunct to existing preventive measures. Once HIV infection occurs, it persists for life. And even with effective antiviral therapy, there may be a lifelong risk of developing AIDS. Primary prevention is, therefore, an essential objective.

Technological advances occurring over the past decade make many approaches to vaccine development potentially feasible. Recombinant DNA techniques have been used to produce viral proteins in E. coli, yeast, insect cells, and mammalian cells. Recombinant live viruses, including vaccinia and adenoviruses, have been constructed that express HIV genes in cell culture and, in the former case, in animals. Synthetic peptides homologous to amino acid sequences of proteins of HIV have been prepared and shown to induce antibodies. Antiidiotype monoclonal antibodies offer another approach under study. HIV-specific immune globulin is under development for use in passive immunization. It is indeed fortunate that the technology exists to make these products so quickly. However, many substantial difficulties remain, including definition of appropriate antigens for use in vaccines and development of methods for demonstrating efficacy.

Most efforts at vaccine development have focused on HIV envelope antigen as the principal immunogen. Both the external gp 120 and transmembrane gp 41, as well as the complete gp160 envelope proteins, have been included in candidate vaccines. Envelope antigen is capable of inducing neutralizing antibodies and can serve as a target antigen for antibody-dependent cell-mediated cytotoxicity and cytotoxic T cells. These immune responses may be crucial for protective immunity. Envelope antigen appears to be important in animal retrovirus immunity. Genetic variation of envelope antigen is a concern, but human neutralizing antibodies are often broadly reactive. The use of HIV core antigen as vaccine is also under study.

Table 1. *Candidate AIDS Vaccines*

Type	Antigen	Source
Subunit	Envelope	Virus
Recombinant	Envelope	E. Coli
DNA-Derived		Yeast
		Mammalian Cells
		Insect Cells
Live Virus	Envelope	Vaccinia
Vectors		Adenovirus
		Herpes Simplex Virus
Synthetic Peptides	Envelope	Solid Phase Synthesis
	Core Antigen	
Antiidiotype	Envelope	Monoclonal
Antibodies		Antibodies
HIV Immune	All	Plasma
Globulin		
Inactivated	All	Virus

Preclinical evaluation of candidate vaccines has involved immunization of a variety of animal species. Neutralizing antibodies have been induced to variable degrees depending on the product and the species. Studies in primates have been considered essential. Chimpanzees are the only animal species which can be infected consistently with HIV. The possibility of using chimpanzees as a model for demonstrating effectiveness of candidate vaccines is still under study. It does not appear that chimpanzees develop AIDS when infected, and the relevance of high-dose intravenous challenge to prevention of human infection is unclear. Promising preclinical data indicate that—even though immunity in animals hasn't been established—clinical studies will likely begin soon.

Clinical studies of AIDS vaccines will occur in phases. The first studies, referred to as phases 1 and 2, will consist of initial evaluations of safety and immunogenicity and definition of optimum immunizing regimens. The complexity of these studies may vary, depending on the product. Evaluation of safety may be more difficult for recombinant vaccinia viruses than for purified proteins. Single doses of some vaccines may be fully immunogenic, while multiple doses administered at intervals over several months may be required for others. The results obtained from animal models and phase 1 and 2 clinical trials will have to provide a basis for decisions regarding which candidate vaccines should be entered into expanded trials.

Definitive clinical trials of safety and efficacy are referred to as phase 3 studies. The size, duration, and complexity of these studies depend on a number of factors. A particularly difficult issue is the question of what the principle objectives of efficacy studies will be. If vaccines prevent infection, the phase 3 studies will be relatively straightforward. On the other hand, if transient or even persistent infection occurs after vaccination, without progression of infection to AIDS, the phase 3 studies will require large numbers of volunteers, will take a relatively long time, and will be complex. Feline leukemia virus vaccine is an example of one that prevents disease without preventing persistent infection. The goal, after all, is disease prevention.

Regardless of what level of efficacy is observed, there are many variables that must be addressed during phase 3 studies. Vaccine efficacy must be addressed in relation to each mechanism of transmission, geographic location, and strain variability. Efficacy for gay men, drug addicts, heterosexual partners, and newborns may differ. It is desirable that multiple safe and effective vaccines become available. Phase 3 of vaccine development is likely to be a multiyear endeavor involving many candidate vaccines, people of all ages in all continents, and people in all risk groups.

Table 2. *Concerns to be Addressed in Phase 3 Trials of AIDS Vaccines*

Safety
Efficacy
Transmissability
Strain Variation
Geographic Variability
Modes of Transmission
Multiple Vaccines

Children represent important and varied target populations for study of vaccine efficacy. Several approaches might be used to prevent infection in newborns.

Table 3. *Potential Methods of Interruption of HIV Transmission to Neonates by Vaccination*

Immunization of at-risk males
Immunization of at-risk females
Infected Spouse
Other
Immunization of Newborn
Ig ± Vaccine

Vaccination of women at risk of infection, such as prostitutes, intravenous drug abusers, and other women partners of infected men may reduce the rate of transmission to newborns. It is not known how often neonatal infections result from transmission of virus at or soon after birth. Those infections which do not occur in utero may be preventable by intervention at birth, perhaps through a combination of vaccine and immune globulin. An important feature of vaccine efficacy trials in newborns is the relatively short incubation period compared to adults. It may be possible to demonstrate disease prevention in newborns more quickly than in older target populations. Fortunately, HIV transmission to children does not occur readily in the family setting. It must be remembered, however, that sexual activity, including homosexual activity, often begins in childhood.

The process of demonstrating vaccine safety and efficacy will be further complicated by related concerns. Target populations for efficacy studies will be people at high risk of infection. It will be necessary to continue to develop methods for prevention in these groups in parallel with clinical trials.

Table 4. *Potential Impact of AIDS Vaccines*

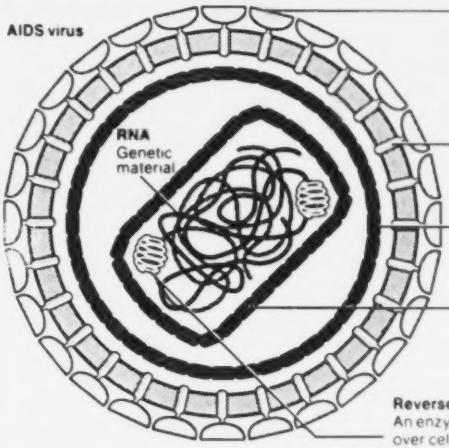
Coverage	Efficacy	Infections Prevented
80%	80%	64%
90%	90%	81%
95%	95%	90%

Practical aspects, such as health care and legal concerns, are also at issue. These related problems will have an effect on the time required to complete efficacy studies. Furthermore, it cannot be assumed that the first generation of candidate AIDS vaccines will be found to be safe and effective. Already, potential approaches to second generation products are being considered and evaluated.

It is impossible to predict exactly when an AIDS vaccine will become generally available. It is certain that the development of an AIDS vaccine will be the best planned and coordinated national and international effort at vaccine development that has ever occurred.

The AIDS Virus: Developing a Vaccine

Once in the body, the AIDS virus provokes production of a range of antibodies that battle it. These do not necessarily protect infected people from developing AIDS. But scientists hope that if a vaccine can induce production of certain antibodies in advance, invasion by the AIDS virus could be warded off. Scientists are trying to locate subunits of the virus that, when injected in the body, will stimulate production of protective antibodies.



GP-110 Also called **GP-120**. A glycoprotein, or sugar-containing protein, that helps the virus attach to and invade cells. Number refers to molecular weight, which scientists label differently.

GP-41 A glycoprotein, also along the outer coat, that plays a role in cell invasion.

P-17 A protein in the inner shell that is suspected to protrude to the viral surface; function is unknown.

P-24 A core protein; function is unknown.

Reverse transcriptase
An enzyme the virus uses to take over cells.

The Current Search

Some experimental vaccines use only GP-120, others use combinations of GP-120 and GP-41 while another uses a synthetic version of part of P-17. Some experts propose using the entire killed virus, but others fear the possibility that some particles could remain alive and cause disease.

The Next Steps

Experimental vaccines are being injected into animals to see which types of antibodies are produced. Since each animal species responds differently and animals do not develop AIDS, these studies cannot reveal whether a vaccine would prevent disease.

The next step is to inject promising vaccines into small numbers of humans to determine safety and the range of antibodies that are produced. At least one French scientist has already done this and American teams plan to soon.

If tests indicate that a vaccine is safe and stimulates production of desired antibodies, complex, large-scale human trials will be started to determine whether it actually protects against AIDS, a process that will take many years.

Once safety and efficacy are determined, a vaccine can be widely distributed.

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A MOTHER'S VIEWPOINT

Mrs. Helen Kushnick

On 13 October 1983, my three-year-old son, Samuel Jared Kushnick, died as a result of Acquired Immune Deficiency Syndrome. After birth, he received twenty blood transfusions from thirteen separate donors in the neonatal unit of a hospital in Los Angeles, California.

Sam's death devastated our family, including his twin sister, Sara. Sam was not the first, but the fourth, premature male to die in Los Angeles during a six-month period, as a result of blood-transfusion-related AIDS. The first was in February 1983, the second in April, the third in June.

When my son died, pediatric AIDS was not considered a disease. I was told that our son's death would not be counted as an AIDS fatality because he hadn't reached the age of five. My husband fought with the hospital administrators, including the head of the blood bank, for 45 minutes after Sam died to have AIDS listed on his death certificate as the cause of his death. What we didn't know was that once the mortuary saw AIDS as the cause of death, they refused to dress his body for burial. The insurance company that provided our medical coverage tried to claim a "pre-existing" condition so that they wouldn't have to pay the $94,000 in medical costs for Sam's 19-day final hospital stay. For six months after he died, I received bills addressed to him on an almost daily basis. They lost. They paid. Then they cancelled our policy.

The first official statistics out of the Centers for Disease Control were published in November 1984. Seventy-two pediatric cases had been recorded. There are now 456 recorded cases of pediatric AIDS, and the pediatric ARC cases are not counted in these statistics.

During Sam's illness, our daughter was ostracized and rejected by a segment of our well-educated, affluent Beverly Hills community. Lack of public awareness of the correct facts concerning the transmission of AIDS caused these people to panic and to force nursery school administrators to expel Sara for fear she could contaminate the other children.

Even after the school and parents had been assured by leading pediatric immunologists and the Los Angeles County Health Department that Sara was perfectly healthy and that AIDS was not communicable by casual contact, the public hysteria persisted, and we were forced to place Sara in another school.

Sara then started kindergarten in a public school. Our applications for private schools had been rejected. Although she had had the required medical examination and inoculations prior to her admission, I was called by the principal and asked for an additional letter from her doctor stating that she was healthy. The school had received a number of calls from concerned parents, even though my daughter was exceptionally healthy and more than two years had passed since her brother's death.

In 1983, my family's decision to go public with our story seemed courageous. To us, it was simply a question of not having a choice. It was clear to us then that AIDS was not a homosexual disease, but a virus.

In my conversations with officials at the Centers for Disease Control in 1984, it was obvious that the number of young victims of AIDS would be growing each

year. Yet the cities have not come very far in the care and education of these children.

Let me tell you about my friend whom I'm going to call "Mrs. Smith." She is black and a single parent. Her three-year-old son also contracted AIDS through a blood transfusion. She has a daughter six years of age. She works as a teacher's aide. She tells no one that her son has AIDS because she doesn't feel she could fight the discrimination and isolation of herself and her daughter were the facts known.

The most horrendous part of this disease is fear and rejection. It is hard enough for an adult to cope with and impossible to explain to a child. This is the end result of our lack of education through proper channels. Until we find a vaccine or cure, the only way to stop the spread of AIDS is through education. We need effective educational programs, designed under the auspices of the Surgeon General, in every city and State in this nation—regardless of how few AIDS cases are statistically counted. As we know, the statistics have been wrong, and ARC cases aren't even being counted. The public must become comfortable with the knowledge that quarantine is not the answer to preventing the spread of AIDS. *Education is.* And not *after* a child with AIDS is admitted to school, but *before.*

The citizens and physicians, practicing and academic, are still not being correctly informed about AIDS. It is not appropriate that both the public and physicians receive most of their medical information through the news media, which has been the case with the AIDS crisis. The majority of the general public does not understand the difference between a specific test for a virus and an antibody test.

While there are now only a handful of post-March, 1985, blood-transfusion AIDS cases, these will surely grow. The same system existing when my son was infected is still in place. Any physician will tell you that blood is a dangerous drug and there is still no standard of care across this nation for blood-transfusion procedures in neonatal units. Yet the population at greatest risk for blood-transfusion AIDS continues to be the children, as the increased cases are showing us.

Most of the local school boards haven't even addressed the issue yet. They wait for crisis situations and then throw the child out of school while they figure out what to do. Shouldn't our citizens be able to go to their government for facts? Aren't the parents of school-age children entitled to receive their facts from the Board of Education?

Government agencies have not effectively utilized educational media, such as television and radio. As a result, the news media has reported its own version of events, which in some instances has been sensational, inaccurate, and has provided little public health information.

And what of the mothers like "Mrs. Smith"? Isn't she entitled to an effective support group? Having a critically ill child is a nightmare, one I hope none of you will ever have to face. The one thing you need most is support.

Statistics show that the highest percentage of pediatric AIDS cases in the years to come will be from IV-drug-user mothers. These children will, in all likelihood, be abandoned in our hospitals. Who will pay for their care? Must these children be abandoned to live in hospitals because there is no residence facility to send them to while a foster home is found? Must the families of children cared for in their own homes be forced underground?

Any facility that receives government funding should not be allowed to discriminate against these AIDS victims.

Response on a Federal and city level to the magnitude of pediatric AIDS has been extremely slow. Please, let us stop dragging our feet, and let us act responsibly now.

During World War II the Federal government with our allies was able to bring together the best scientific minds in the world to develop the atomic bomb. Well, we are at war now and our allies are the world health community. We need to bring together the best scientific minds in the world—not just in our country—to fight this killer. We need the best researchers, clinicians, and scientists under the same roof on a daily basis. We cannot continue to ask these people to spend months filling out grant applications to fund their work.

Three years ago I made a promise to my daughter. She became frightened one evening that she couldn't remember Sam's voice—afraid that she was beginning to forget him. I promised her then that her father and I would not let Sam be forgotten. You see, we hear his voice all the time.

WORK GROUP RECOMMENDATIONS

INTRODUCTION TO WORK GROUPS

The participants invited to the Workshop were assigned to ten Work Groups composed of approximately twenty persons. Group members were selected to reflect a broad range of background, expertise, and diversity of opinion. The Planning Committee provided the leaders and recorders in advance a set of charges herein summarized as "Definition of the Issues." With these issues as a starting point, the groups met in closed session for ten hours over a two-day period. Discussion was spirited. In most instances, consensus about current knowledge was reached, and recommendations were made for future action.

In a closing plenary session each group leader presented a summary of the group's deliberations to the Surgeon General. A condensation of these follows under "Response of the Work Group." The Surgeon General responded to these presentations in the conference's final hour.

WORK GROUP I: NATURAL HISTORY OF PEDIATRIC HIV INFECTION, INCLUDING DEVELOPMENTAL ISSUES AND PROGNOSIS

DEFINITION OF THE ISSUES:

The clinical presentations of HIV infection in children and infants, whether acquired perinatally or from blood or blood products, are quite variable. As a result, there has been inadequate definition and classification of the clinical course and prognosis, particularly with relation to differentiation of AIDS-Related-Complex (ARC) and progression to Acquired Immunodeficiency Syndrome (AIDS), Central Nervous System (CNS) disease, and death. Populations followed at different centers vary in terms of socio-economic background, clinical presentation, and medical management.

RESPONSE OF THE WORK GROUP:

The mechanisms of transmission of HIV from mother to offspring are unknown. Intrauterine transmission is well-documented, but the time at which intrauterine transmission occurs, the importance of evidence of additional maternal infection, the factors which influence risk of transmission, and the factors that

modify outcome of transmission are not understood. Available data to date have not shown a clear correlation between clinical status of the mother and the effect of HIV exposure to the infant. Some observations suggest that mothers in the late stages of AIDS may not infect their infants to the same degree as mothers who are asymptomatic or less severely involved.

In general, infants who are symptomatic early in life following intrauterine infection or from infection after transfusions in the neonatal period will have more devastating courses than those children who are asymptomatic in early infancy or those who acquire their infection through later transfusion or through administration of blood factors.

Laboratory abnormalities in pediatric HIV infection are now well recognized, but their significance in prognostic terms will be determined only through prospective longitudinal study. B-cell dysfunction may appear early and is associated with hypergammaglobulinemia. The development of lymphopenia, hypogammaglobulinemia, T-cell mitogen abnormalities, depression of both T4 and T8 cells, and loss of antibody to P24 (core antigen) suggest disease progression and probably are poor prognostic signs. In addition, there is a group of patients who are seronegative but have positive cultures; the significance of these findings is unclear.

Developmental issues are a major concern in pediatric HIV infection. Patterns include the infants who fail to progress in normal developmental sequence and those who develop normally initially but then either reach a plateau or deteriorate with loss of milestones. Primary CNS infection due to direct HIV invasion occurs in children as in adults. It can be difficult to distinguish the cause of developmental delay which may be secondary to sociocultural factors or recurrent opportunistic infections or from primary invasion of the CNS.

Whereas much has been learned about the clinical manifestations of HIV in infants and children, our knowledge is biased toward the common and severe expressions of the infection. Broad based study is required to obtain wider perspective.

RECOMMENDATIONS:

1) Long-term, controlled, prospective collaborative studies of the natural history of HIV, including assessment of clinical course and laboratory findings in children, are required now as a basis for development of effective means for prevention, diagnosis, and treatment. Appropriate government funding agencies should assist and even require development of common and shared protocols. Studies should include, but not be limited to: a) the roles of co-factors such as Epstein-Barr virus and other herpes viruses; b) strain differences in HIV and their relationship to clinical manifestations; c) distinctions between lymphoproliferative and lymphoablative disease with opportunistic infection; d) the prognostic significance of low incidence complications in pediatric HIV, such as cryptosporidiosis, Mycobacterium avium-intracellulare, and Kaposi's sarcoma; e) analysis of cerebrospinal fluid, including specific antibodies, cell mediated immunity, and antigens; and f) the roles of psychosocial and nutritional factors in the underprivileged populations which are at highest risk.

2) Denominator data are essential. Mandatory screening of all newborns is *not* recommended. Instead, limited screening studies, building on the existing neonatal screening programs for metabolic disease and sickle cell disease, should be implemented to help define the geographic seroprevalence of HIV infection.

3) Programs should be funded to explore ways to provide broad prenatal and neonatal testing for identification of HIV infected individuals. The programs should be initiated with sensitivity to the special dimension of HIV infection, especially regarding privacy and informed consent issues.

4) High priority should be given to development and evaluation of laboratory tests for identification of HIV infection in newborn and young infants. Particular attention should be given to longitudinal study of cerebrospinal fluid. The special vulnerability of the newborn, the irreversibility of brain damage caused by HIV, and the potential for benefit from early treatment (including the treatment of the asymptomatic HIV infected infant), give urgency to the need for sensitive, specific, and practical tests.

5) The CDC classification of pediatric HIV infection should be used to insure that all children with HIV infection are eligible for needed services not limited by statutory or regulatory definitions of AIDS. Continual updating of the classification can result in a useful transition document for education of health professionals and the general public about HIV infection.

6) Study of pathologic specimens from pregnant women and from children with HIV infection can make major contributions to understanding the natural history. These studies should include specimens of placenta, chorionic villi, products of conception, amniotic fluid, and cervical secretions. Professional education programs, based on existing successful models, should be created to assist in obtaining and studying such specimens. Consultational assistance by authoritative pathologists and clinicians should be included as part of the program.

7) Adolescence is a time of special hazard, but can be the focus of special opportunity for prevention of HIV infection. Recognizing the complexity of this problem, we recommend the prompt convening of a group to focus on the specific problems of HIV infection in adolescents.

WORK GROUP II: THE TREATMENT OF CHILDREN WITH HIV INFECTION

DEFINITION OF THE ISSUES:

The status of medical therapies for HIV infection, their indications and timing, their complications, and their sequellae are unclear. A number of drugs have been proposed for use in various stages of HIV infection, but their indications have not been developed for pediatric cases. The current therapies for secondary infections, such as pneumocystosis, cryptosporidiosis, and atypical mycobacterial disease, are generally unsatisfactory. Appropriate indications, dosages, and timing of antibiotics and gamma globulin need to be defined. Newer therapies, such as immunomodulators, may eventually have a place in pediatric management. Mean-

while, HIV infected children, though often immunosuppressed, will face the usual pediatric problems of immunization against childhood diseases and management of viral infections such as varicella and measles.

RESPONSE OF THE WORK GROUP:

It is imperative to determine the most beneficial therapies for children with HIV infection carefully and as quickly as possible. Children have the right to participate and must be included in therapeutic trials, so that appropriate treatment can be offered them.

There must be formed a well-funded, single collaborative pediatric treatment group, using the existing AIDS treatment and evaluation units as a foundation and incorporating the pending clinical studies groups. Our group recommends the designation of an executive director to assure efficient and rapid formulation of well-designed protocols for optimum utilization in the known HIV pediatric population. Our group also suggests that a commitment of a minimum of 12 million dollars annually to pediatric AIDS therapy is necessary for implementation of these recommendations.

Protocols for collaborative controlled Phase II trials of drugs such as azidothymidine (AZT) and ribavirin (Virazole) in children with AIDS must be ready for initiation as soon as the pharmacokinetic data from the current Phase I studies become available. Placebo-controlled trials in HIV-infected children with AIDS-Related-Complex (ARC) and in asymptomatic children must be designed in parallel with the above studies and implemented when appropriate data have accrued. The collaborative group also should begin now to design treatment trials in seropositive pregnant women and of infants born of such pregnancies to attempt prevention or, at least, intervention in the course of perinatally acquired infection. Natural history data and carefully evaluated diagnostic tests will facilitate the implementation of such studies.

RECOMMENDATIONS:

1) A controlled trial of intravenous gamma globulin therapy in conjunction with specific anti-HIV therapy would be useful but should not be done at the expense of decreasing available patient populations for the more important specific anti-HIV trials.

2) At a later time, specific use of immunomodulators in conjunction with specific antiviral therapy can be considered, but available data suggest a low priority currently.

3) Pneumocystis carinii pneumonia (PCP) is currently treated with trimethoprim-sulfamethoxazole and/or pentamidine. Evaluation is needed of aerosolized pentamidine, newer agents of the dihydrofolate reductase antagonist class, and of prophylactic therapy.

4) Lymphoid interstitial pneumonia (LIP) is a major problem. Combined therapy with steroids and specific antiviral agents needs evaluation.

5) Candida infections, including esophagitis, require systemic therapies, including amphotericin and imidazoles.

6) Cytomegalic virus (CMV) infections are difficult to manage, but new acyclovir analogs (gancyclovir) warrant Phase I and II evaluation. Children who are HIV-positive but CMV-negative should receive CMV-negative blood if transfusion is indicated.

7) Cryptosporidiosis and atypical mycobacterial infections are relatively infrequent in children. No effective therapy currently exists for them. Efforts should be directed toward finding treatment.

8) We support the current Advisory Committee of Immunization Practices (ACIP) recommendations for immunization of HIV-positive children. The use of age-appropriate inactivated antigens, such as DPT, pneumococcal, Hemophilus influenzae B, and influenza, is potentially beneficial in those HIV-positive children capable of responding to the antigens. These are without harmful effects. Administration of attenuated measles vaccine is recommended for asymptomatic HIV-positive children. It appears to be without hazard in this group of patients and may provide protection against wild measles virus, which is potentially lethal. Symptomatic HIV-positive children should not receive live virus vaccines. HIV-positive children exposed to measles should receive gamma globulin. Those exposed to varicella should receive varicella zoster immune globulin.

9) Management of HIV-infected patients with varicella should include acyclovir therapy. Patients with varicella, measles, and respiratory syncytial virus infections are extremely susceptible to bacterial superinfections, such as pneumonia and sepsis.

10) Indiscriminate use of antibiotics should be discouraged, but well planned studies of antibiotic prophylaxis would be helpful.

11) Nutrition and growth must be monitored carefully. Enteral tube feeding and total parenteral nutrition must be maintained appropriately. Irradiated blood, if available, should be administered when indicated.

12) There is a pressing need for experienced pediatric subspecialists to care for these children. We strongly support the training of these individuals.

WORK GROUP III: RISK REDUCTION FOR MATERNAL/FETAL TRANSMISSION

DEFINITION OF THE ISSUES:

The predominant paths of HIV infection transmission from mother to child are not understood. The effect of pregnancy on the health of the infected mother is uncertain, as are the effects of the infection on the outcome of pregnancy.

Eighty percent of American children with AIDS are of black or Hispanic parentage. Their mothers are predominantly of lower socioeconomic status, and most often are intravenous drug abusers or sexual partners of men in high-risk categories. Counseling of HIV-infected women, when achievable, must consider these factors and center on understanding the risk of pregnancy, birth control methods, informing sex partners, and issues of confidentiality. There are no satisfactory guidelines for HIV antibody testing of women of child-bearing age with known risk factors.

RESPONSE OF THE WORK GROUP:

We define these general points as background to our recommendations.

a) In a series of "life-points," each offers opportunities for education and risk reduction. Some of these occur during adolescence or even earlier, some at the time of premarital and family planning counseling, and some during preconceptional, antepartum, intrapartum and postpartum care.

b) The concept of "parental-fetal" transmission (rather than "maternal-fetal") emphasizes the role of the male partner in infecting the mother and through her, the fetus.

c) Adolescents are an especially important target group for risk reduction efforts. There is a need to design relevant approaches to them, perhaps through the use of peers and/or popular role model adults.

d) It is important to stress that transmission to the fetus is currently very strongly linked to inner-city, disadvantaged, minority populations. The connection between poverty, intravenous drug abuse, and heterosexual transmission leading to fetal infection underscores the importance of a massive effort against the primary problem of substance abuse.

e) The young, drug-addicted, infected prostitute is more at risk for pregnancy and fetal infection. North American evidence of transmission of HIV from prostitutes to "Johns" to their other sexual partners and from bisexual men to heterosexual females needs to be determined by thorough epidemiologic investigations.

RECOMMENDATIONS:

1) There should be a vigorous expansion of HIV-antibody testing, always within a context of confidentiality, voluntary informed consent, and pre- and post-test counseling. The group sees no current role for mandatory testing or screening under any circumstances, but counseling and testing should be routinely offered to all pregnant women as early in pregnancy as possible. For those who have negative tests, testing should be offered again late in the third trimester, at least three months after initial testing to allow for important pediatric management and follow-up.

2) Risk assessment and access to counseling and testing should be widely available at such points as family planning clinics, sexually transmitted disease clinics, abortion clinics, drug treatment clinics, and at all health care centers for women and their sex partners. Major funding investments are urgently needed for counseling resources, and health professionals must take a much more active and knowledgeable role.

3) HIV infection status should be part of the medical record. The group was divided as to whether test results should be in the generally available chart. Strict confidentiality must be observed, but the information must be available for appropriate obstetrical and pediatric care. Maternal HIV status is relevant to newborn care and ideally should be discussed in confidential consultation between physicians, especially obstetricians and pediatricians. Strong legislative protection of confidentiality and against discrimination is urgently needed on a State-by-State basis, and the possibility of Federal legislation should be examined. Expanded AIDS education is needed by all members of the health-care team.

4) With regard to antibody test outcomes: a) presentation of test results, whether negative or positive, should be accompanied by counseling regarding

risk-avoidance; b) the seropositive pregnant woman should be provided information on the full range of risks to herself and to her offspring, should have access to the full spectrum of options (including termination of pregnancy) in a nonjudgmental, noncoercive context, and should receive the support of health care providers if she decides to continue her pregnancy; and c) the seropositive nonpregnant woman should be advised to defer pregnancy. There should be sensitivity to the difficulties faced by many women in avoiding pregnancy.

5) Although definitive evidence for HIV transmission through breast milk has been lacking, the documented presence of HIV, both within lymphocytes and in cell-free breast milk, suggests that it is prudent to advise seropositive women not to breastfeed, especially in North America, where formula feeding is a safe alternative. Donors of breast milk should be screened for HIV infection.

6) Available risk-reduction modalities, such as use of condoms and use of sterile syringes and needles for intravenous substance abusers, must be made more easily accessible.

7) Sperm donated to sperm banks for artificial insemination should be made as safe as blood donated to blood banks by mandating statutory requirements for collection and freezing of the sperm.

8) Mandatory premarital HIV antibody testing would not be appropriate and would probably be ineffective in reducing HIV infection. However, premarital risk assessment, counseling, and voluntary testing should be encouraged.

WORK GROUP IV: EDUCATIONAL ISSUES FOR CHILDREN ALREADY INFECTED WITH HIV, INCLUDING DAY CARE AND SCHOOLING

DEFINITION OF THE ISSUES:

Much confusion and fear cloud the issue of the safest and most effective means of educating the HIV-infected child. The consternation accompanying association with HIV-infected individuals is perhaps most marked with the enrollment of an infected child in day-care centers and schools. Proper education, confidentiality, and safety for infected children—particularly those who are immunosuppressed—and their non-infected schoolmates must be considered. School boards, school principals and directors, teachers, and families need sensible, realistic guidelines based on the best current knowledge. Resources must be developed for dissemination and implementation of new information as reported.

RESPONSE OF THE WORK GROUP:

Education of the HIV-infected child should be geared to developmental age. We considered those under age five as preschoolers and also distinguished toddlers from three- and four-year-olds. Positive messages about education should be based on known epidemiology and stage of disease. There are children known to be HIV-infected yet asymptomatic, those with unrecognized infection, and those ill with HIV and dying. All of these may be attending school or may be rejected from school if their medical history were known.

RECOMMENDATIONS:

1) There is no evidence that HIV is transmitted by normal casual and nonsexual contact in home, school, day care, or foster care settings. Screening of children for the presence of HIV antibodies for the purpose of attendance at day care centers or school is neither warranted nor recommended. Routine common sense procedures for handling blood and body fluids should be adopted for everyone. The decision to inform others of HIV infection should only be made with the consent of the parent and/or guardian. Although it is ideal that someone in day care or school know that a child is ill, that should not be a prerequisite for attendance and may not be practical at this time in many communities.

2) Existing Centers for Disease Control (CDC) and American Academy of Pediatrics (AAP) guidelines are well done and serve as an adequate resource in most respects. However, the group recommends the following modifications:

a) If infected toddlers can safely mingle with peers, that should be so stated. If there is evidence they can transmit HIV infection to each other, that evidence must be clearly presented. We have not seen any data that toddlers can transmit HIV infection. CDC comments on the preschool population are somewhat ambiguous. CDC should reanalyze data or design new studies if existing data cannot be brought to support clearer recommendations one way or the other.

b) We do not agree with the Academy's suggestion that an expert panel review toddler admissions to day care. The child's own physician and parents can make a reasonable decision. Community school boards and departments of health may make a panel available if physicians, parents, or teachers request expert advice. The child does have the right of privacy. Doctors should share data on HIV infection with others only upon careful consideration of likely community reaction and with parental consent. This right to privacy extends to a child attending preschool or day care.

3) The following are our suggested criteria for admission to school. For children of developmental age three years and up, there is no need for special school admission criteria. HIV-infected children should be permitted to attend school unless prevented from doing so by weakness or poor health. For preschoolers less than age three and for older children developmentally less than an age three equivalent, we suggest a more positive national position. Hedging at the national level may lead to fear at the local level. Again, CDC should reexamine the accumulated data and either make a more positive statement or quickly gather data about transmission between toddlers.

4) Under ideal circumstances, the teacher or someone in the school should know the diagnosis and be an active participant in the team caring for the child. In many communities, however, it may not be possible for the child to attend school in an unrestricted manner if the diagnosis is known. The child has the

right, therefore, to have the information withheld from the school. The decision as to whether an immunocompromised child can attend school safely, with the unavoidable exposures to enteric and respiratory ailments, is best left to his own physician and caretaker. Schools need to notify all parents about outbreaks of illnesses such as measles and varicella, which pose a particular threat to immunocompromised children.

5) Whenever possible, school systems should be prepared ahead of time by education of staff, parents, and social workers, to accept an HIV-infected child should one be identified. Current hygienic measures are sufficient in most school and preschool settings, and handwashing facilities always should be accessible. If soap and water are sufficient to clear up blood spills, this should be stated in published guidelines which currently tend to emphasize the need for bleach. Positive hygienic measures should be clearly stated and adhered to consistently.

6) Children with HIV infection should share the same curricula as their uninfected schoolmates, including age-appropriate health and sex education. Counseling regarding sexual behavior for HIV-infected adolescents should focus on risk reduction and modes of transmission. There must be age-appropriate education about AIDS for all children: common sense information about body functions in preschool years; counseling about decision making and developing self esteem in elementary school; specifics about risk reduction and transmission before the age when a child begins to experiment with sex and drugs.

7) Use of the antibody test in children must be done with prudence and for reasonable clinical cause. The group opposes mandatory testing prior to school attendance.

8) Ultimately, it should become possible for AIDS to be considered with neither more nor less emotion than other severe illnesses of infancy and childhood. Key issues of AIDS epidemiology are poorly understood by most segments of society. A concerted community educational effort should be undertaken. Guidance and education programs developed with Federal support should be directed from national groups to their memberships, including health-care groups, education and parent groups, and social work groups.

WORK GROUP V: THE ROLES OF EPIDEMIOLOGY AND TRANSMISSION STUDIES IN THE ADVANCEMENT OF KNOWLEDGE OF PEDIATRIC HIV INFECTION

DEFINITION OF THE ISSUES:

The incidence of congenital HIV transmission is closely related to the spread of HIV infection among intravenous drug users and their sexual partners, partners of bisexual men, and – to an increasing degree – among the heterosexual population. Other children at risk include: neonates, those with blood dyscrasias who have received multiple transfusions, hemophiliacs managed with blood products, children with cardiac anomalies repaired by surgical by-pass, and sexually abused children. The routes involving vertical (adult-to-child) transmission need proper quantification. Further studies are needed to provide information and projections about the course of the epidemic.

RESPONSE OF THE WORK GROUP:

The current national reporting of pediatric AIDS is only a very small reflection of the total problem of HIV infection in infants and children.

The current annual number and distribution of HIV-infected women and HIV-infected infants can be estimated by utilizing available data from area-specific HIV antibody surveys and by extrapolating from reported AIDS cases in adult females. Such estimates in early 1987 placed the number of HIV-infected women at about 100,000. About 70% of these were from minority groups in New York, New Jersey, and Florida, with 80% of the infections attributed to intravenous drug use by the infected woman or her sexual partner. By applying published age, race, and specific fertility rates to this estimate, we calculated that about 3,000 HIV-infected infants may be born annually in the United States. The number of both infected women and their infants can be expected to increase over the next several years. However, accurate projections of the rate of increase are not possible at this time because of major uncertainties in key variables.

Studies in Massachusetts and New York show prevalence of HIV antibody in pregnant women ranging from 2% up to 6%. The Massachusetts Department of Health has developed an anonymous, confidential screening test using blood specimens collected on filter paper for newborn metabolic screening. Patient identification was removed, but race and general geographic area were retained. Testing of these specimens provided valuable data on the general prevalence and distribution of HIV-infected women giving birth and their infants. Other States should consider inaugurating this method so that intensive follow-up and educational programs can be targeted to the high prevalence areas.

RECOMMENDATIONS:

1) The majority of our group felt that mandatory premarital testing would not be effective, but that voluntary testing, with pre- and post-test counseling, should be offered at family planning clinics, sexually transmitted disease clinics, and drug abuse treatment programs.

2) Insufficient data are available to indicate what proportion of infants may be infected in utero or at birth, and what maternal factors may be important for transmission of HIV infection to the offspring. The group recommends convening a meeting of those investigators involved in current or prospective studies of HIV-infected pregnant women to develop additional protocols to answer important questions regarding maternal-fetal transmission.

3) With respect to the possibility of infection by an HIV-infected toddler to other toddlers in a day care setting, we conclude that if such a transmission risk exists at all, it would be an exceedingly low one, and that such a non-risk or low risk would be difficult if not impossible to measure by a prospective epidemiologic study. However, guidelines and a specific protocol should be developed by CDC to direct a public health investigation when such is warranted.

4) Donors of breast milk should be screened in a manner similar to donors of either blood or body organs. When environmental circumstances are such that withholding breast milk might be associated with a known increased risk of morbidity and mortality, breast milk should not be withheld even though there may be potential incremental risk of HIV transmission from an infected mother to her infant.

5) The risk of HIV transmission through blood transfusion in the period before screening (specifically between 1979 and 1985) appears low enough that routine recall for testing of children who received blood appears unnecessary. We concur, however, with the recent CDC recommendations that screening based on geographic areas and number of units received may be appropriate.

6) HIV testing should not be done routinely on all children admitted to health care facilities, but it should be performed when there are specific clinical and epidemiologic indications to suspect HIV infections. Protocols for evaluation of a child who has been sexually abused should consider the possibility of HIV transmission.

7) The collection and interpretation of epidemiologic and transmission studies must be sensitive to different ethnic and cultural groups. The press and general public must understand that the nature of scientific studies prevent public officials from implying that an "unlikely" event will "never" occur.

WORK GROUP VI: FAMILY ISSUES, INCLUDING COUNSELING AND PSYCHOSOCIAL ISSUES

DEFINITION OF THE ISSUES:

The potential for stigmatization complicates the health and social care of the HIV-infected individual at any age. In particular, school-aged children with HIV infection become the focus of fears of teachers, classmates, and neighbors. The result may be ostracism, discrimination, and low self-esteem. Many of these children are already the victims of drug-abusing parents, paternal bisexuality, and low socioeconomic status. About 15%, however, became HIV infected by

receiving HIV contaminated blood or blood products. Many will not survive to school age. Counseling of the children and the families of these differing subsets of patients must necessarily be adapted to the circumstances. Counseling must aim at providing psychosocial support for families, discussing pregnancy risk, and reducing high-risk behavior. The demography and social dynamics of HIV infection should be studied thoroughly to develop effective means of reaching people at risk, to delineate the obstacles to behavioral change, and to determine an effective language and style of communication.

RECOMMENDATIONS:

1) We suggest that a continuum of services be assured to all affected communities by the Federal government, working through State and community facilities. These services must range from fundamental necessities, such as food, shelter, transportation, and mainstream education to the critical needs for emotional and other psychosocial support services. We believe that it is a Federal responsibility to provide a structure for leadership and funding for local planning and program development. The organization, development, and implementation of psychosocial services must be considered of equal importance to medical services with a corresponding allocation of funds.

2) Direct services to families with HIV-infected children should be planned, organized, and implemented by a community-based, child-centered multidisciplinary team, consisting of representation from health and social service specialties, augmented by community service representatives and family members. Services should be geared to family assessment in its own ethnic and cultural context with consideration for its religious orientation and spiritual needs.

3) Throughout the process of working with a family affected by pediatric AIDS, a consistent counseling relationship establishing respect and mutual trust must be maintained. Professionals must be aware of and sensitive to cultural issues, sexual and reproductive mores, and psychosocial aspects of drug abuse. Psychosocial personnel must be recruited from appropriate minority groups with bilingual counseling available as needed. All involved Federal and State agencies should establish training of involved personnel as an immediate priority.

4) We urge expanded access to drug treatment services and increased funding for such services to improve quality and to remove financial barriers.

5) It is essential that families have a clear understanding of proposed medical and social interventions given in their own language, and that they be afforded the opportunity for a truly informed consent. Although family involvement should and must be encouraged, adolescents must be provided the opportunity to obtain services independent of parental knowledge and consent.

6) It is critical that minority representation be included at policy-making levels. We recommend that the Surgeon General take the lead in providing a forum of prominent black and Hispanic/Latino leaders, especially physicians, to be heard on a national level.

7) Planning for research in the areas of psychosocial interventions, health care service delivery, and services evaluation should include local community representation, with the Federal government assuming a leadership role in the dissemination of acquired information.

8) CDC should revise guidelines on education and foster care and on perinatal transmission to incorporate the psychosocial, cultural, and ethnic factors discussed above.

9) Cultural, racial, ethnic, gender, and psychosocial issues should be specifically addressed at all future national conferences on HIV infection, as they have been at this one. This is necessary for a broadening of the understanding and communication of all professionals working in the field.

WORK GROUP VII: HEALTH INFORMATION ISSUES AND THE ROLE OF THE MEDIA

DEFINITION OF THE ISSUES:

The standard print and electronic public media, in concert with profit and non-profit health information services, are the means by which information about AIDS is disseminated to the general population. The media must both receive and transmit accurate information in a responsible manner. This information must reflect, but not be confined to, current knowledge and epidemiology, natural history, transmission of the disease by mother to child or by blood and blood products, treatment, and research in the development of drugs and vaccines. Even more important, the media are essential for the dissemination of information to minimize the spread of the disease, including modifications in life style, the understanding of high-risk sexual behavior, and the risks of pregnancy for the HIV-infected mother. Such preventive information must be adapted to reach those cultural, ethnic, and social groups most at risk. Methods should be developed for evaluating the effects of health information systems on public knowledge and habits.

RESPONSE OF THE WORK GROUP:

The group felt that there are certain specific steps that would improve the effectiveness of communication regarding HIV infections and AIDS. First, it was felt to be essential that ambiguities and imprecision be avoided in terminology and jargon. Meaningless euphemisms, such as "the exchange of bodily fluids," should be abandoned in favor of clear and explicit language.

Because journalism has unique responsibilities differing from other forms of mass communication, we have developed separate recommendations for the news media. The professional journalists on our panel felt it inappropriate for them to make policy recommendations about subjects which they cover.

RECOMMENDATIONS:

1) Current information campaigns often seem to define risk for AIDS by membership in specific groups, rather than by high-risk behavior. This approach serves to increase stigmatization and discrimination and undermines the public's understanding of health risks. We urge the government to take the lead in helping to reverse this trend.

2) A panel independent of government and consisting of journalists and other authorities in the communication field should be convened under the aegis of a group such as the National Academy of Sciences or the Institute of Medicine. The panel should include individuals with expertise in communicating with those target segments of the population for which AIDS is a particular concern. A media resource guide should be developed by such a panel. This should include, but not be limited to, such AIDS information sources as research scientists, government agencies, legal and civil rights organizations, social service organizations, and health care associations. Data bases, such as the Scientists' Institute for Public Information (SIPI) or the Computerized AIDS Information Network (CAIN), are particularly valuable.

3) This panel should stimulate the development of a style book to address the use of ambiguous ("sexually active"), judgmental ("promiscuous"), or stigmatizing ("innocent victims") language. The publications of the panel should be distributed widely to journalists and to other communicators.

4) The panel also should explore the issues of confidentiality in reporting of AIDS. These issues must include the needs of journalists for information, the public's right to know, the right to privacy for persons with AIDS, and the responsibilities of health care providers and social service workers to serve the needs of their patients and clients.

5) Significant portions of the population, including intravenous drug users, adolescents, those with language barriers, some homosexuals, and poorer individuals, are not being reached with the educational messages that are conveyed through traditional media. The techniques of market research should be used to identify the most effective means of communicating with all parts of the population, and alternative communication resources should be explored for the dissemination of information about AIDS. These should include direct mail, explicit television public service announcements or educational spots, posters on busses and subways and at rock concerts, comic books, as well as the integration of information concerning AIDS and responsible sexual practices into all television programs, including entertainment. Messages should be targeted for specific publics, with recognition of linguistic, cultural, societal, and age differences.

6) Specifically, the public and private sector should work in concert to:

a) translate public information programs into appropriate languages, such as Spanish;

b) improve communication with the black community by assembling an advisory group of black leaders from the community, the clergy, health providers, and the media;

c) urge Hispanic/Latino leaders of the medical profession and electronic media to take the lead in the education of their communities;

d) enlist black and Hispanic/Latino opinion leaders and role models to deliver educational messages through appropriate mass media; and

e) disseminate information about HIV risk to intravenous drug users through urban community and outreach programs.

WORK GROUP VIII: MODEL FOR HEALTH CARE OF CHILDREN WITH HIV INFECTION, INCLUDING BOTH IN- AND OUT-OF-HOSPITAL CARE

DEFINITION OF THE ISSUES:

The disadvantaged and underserved children most at risk for HIV infection are also at greater risk for many other diseases and conditions. Their health care is typically fragmented, episodic, crisis-oriented, and underfinanced. They usually are denied a relationship with a primary physician who might assume responsibility and accountability for their health. Their care is often complicated by parental intravenous drug abuse, parental HIV-related infection, homelessness, and abandonment. There is a lack of foster-care placements, resulting in prolonged stays in hospitals, where there is insufficient staff to provide and coordinate multidisciplinary attention. Pediatric units in hospitals that serve large numbers of HIV-infected individuals are overwhelmed by the medical and social needs of ill and potentially ill HIV-infected children. Programs which provide coordinated, community-based care and hospice environment for pediatric HIV-infected patients are nearly non-existent.

RESPONSE OF THE WORK GROUP:

The development of a model of health care for HIV-infected children demands that we, who are responsible for their care, face the complexities of poverty, its resultant social disorganization, and the attendant hopelessness. Pediatric HIV infection is commonly related either directly or indirectly to intravenous drug use. Because the resources for the prevention and treatment of drug abuse are insufficient to meet the needs of this country, we encourage everything possible to expand treatment and prevention programs dealing with drug abuse.

RECOMMENDATIONS:

1) The Department of Health and Human Services (DHHS) should initiate efforts to simplify access to existing health, welfare, social, and financial services for HIV-infected children and their families.

2) Whenever possible, these children should remain with their own families. The provision of social and medical supports – including but not limited to housing, home care, and respite care – will help preserve, as much as possible, the family unit and reduce the need for foster care. Existing systems for handicapped or disabled children must be made accessible to HIV-infected children.

3) When care of the child within the family is not possible, individual foster care represents the best possible alternative. We suggest increased foster care funding, along with additional social and practical supports such as day care and home care, in order to recruit larger numbers of badly needed foster parents.

4) The recommendations for increased supports for the natural family, or if not possible, for the increased recruitment of foster families will not successfully provide care for all HIV-infected children. Innovative nurturing homes for small numbers of HIV-infected children should be established. In these community-based homes, children would be cared for by appropriately trained and super-

vised caregivers who will bond with and care for the children and, if possible, their parents.

5) Regionalized, comprehensive medical care programs tailored to regional needs should be instituted. These should use a multidisciplinary team approach to provide primary care for HIV-infected children. Services should be provided with a greater emphasis on location of patients rather than on location of traditional tertiary care services. Obviously this model will have to be tailored to individual regions, but must include attention to the education of local health care providers about clinical and social needs of HIV-infected children and their families. At the medical level, these children need a pediatrician with the instincts of a primary care provider and a broad perspective. They must also have highly trained nurses and social workers to facilitate, negotiate, and coordinate services for them.

6) We recommend that health care providers and Federal, State, and local policy makers enlist the local minority leaders and community organizations in the development and implementation of programs for HIV-infected children. Such cooperation is necessary as we develop a national strategy.

7) In those sections of the nation with either little or no pediatric AIDS now, community, government, and professional leaders in health, public health, and human services should begin immediately to plan for the care of the HIV-infected children who will inevitably appear in the near future.

Certain metropolitan centers have increasingly large numbers of antibody-positive infants, many of whom do not have homes to which they can be sent. Hence these recommendations have an urgency ignored only at our peril. Over the last six years, all of us have been forced to deal with problems perhaps better appreciated by health professionals of 50 years ago, but unknown to us since the advent of antibiotics. There is much we do not understand about this disease, but we do have enough knowledge to treat these children and their families so that the quality of their lives is improved. Since many children afflicted with AIDS are poor, it is our responsibility to ensure that they receive the medical and social care they need to live humane and civilized lives. It is our moral obligation to do so.

WORK GROUP IX: FINANCIAL ISSUES IN THE CARE OF CHILDREN WITH HIV INFECTION

DEFINITION OF THE ISSUES:

The AIDS epidemic will impose incredible economic burdens at the international, national, State, local, and family levels. In many areas, hospitals, blood banks, and local governmental and social service agencies already are being strained financially. Methods have to be found for accumulating data, raising sufficient funds, and developing channels for support for all aspects of prevention

and treatment of pediatric AIDS. We must take into account the increasing number of cases, the need for increased prevention programs, and inflation. The peculiarly pediatric issue of abandoned HIV-infected babies must be considered. Suggestions for protocols and legislation for cohesive programs must be outlined to allow governmental and quasi-governmental agencies, foundations and other non-profit organizations, third-party payers, hospitals, corporations, families, and individuals to promote cooperative economic strategies.

RESPONSE OF THE WORK GROUP:

While the increased funding for research and education in response to the AIDS epidemic is to be applauded and encouraged, we need to pay more attention to financing the delivery of treatment and related social services for those already infected and those who may become ill.

RECOMMENDATIONS:

1) Because reliable data are scarce, we can make only rough estimates of the health care costs of pediatric HIV infection. Given the limitations of the current surveillance definition of AIDS and the underreporting, a projection of 10,000 pediatric cases with symptomatic HIV infection by 1991 seems probable. A number of studies has found hospital utilization of 30 to 40 days per year per child. For those children who cannot be discharged because of extraordinary placement and care problems, the figures are much higher. We estimate that by 1991 between 800 and 1,000 hospital beds, representing 2% of the nation's pediatric beds, may be needed. The impact will be much greater in the high-prevalence areas for pediatric AIDS, such as Newark, New York City, and Miami. Obviously, there are also other costs, including drugs, home care, ambulatory services, and foster care. The care must be multidisciplinary and must involve thorough coordination across a wide range of services and settings.

2) Our financing strategies must be designed to support and encourage alternatives to hospital care whenever possible. We cite two examples:

New Jersey is the first State to develop a "Home and Community Based Services Model Waiver for Persons with AIDS/ARC" under the Medicaid program. Under this waiver, New Jersey has elected to provide services such as foster care, case management in a community-based setting, private duty nursing, medical day care, personal care assistance supervised by a registered nurse, and drug abuse treatment. This brings Federal matching dollars into the State for multidisciplinary services not normally covered under Medicaid.

In New York State, designated AIDS Care Centers receive an increased reimbursement rate for enhanced care to AIDS patients. The goals of the program are to improve the patients' quality of life and to reduce in-patient care through maximum utilization of ambulatory services. Some of these facilities include specific pediatric AIDS services providing family support and linkages with community programs. The program has an evaluation and financial data collection component.

3) AIDS often strikes those with the least ability to pay and may affect entire families. Many of the required services are not covered by either public programs or private insurance. Approved drugs, like AZT, may cost $10,000 per patient per year and often are not covered by private or public programs. Some changes

in our current method of financing health care clearly are needed. The recommendations of our group are based on the idea that all segments of the health care financing system should share the cost of HIV-related illness.

4) We support legislation which would waive the 24-month disability waiting period for Medicare eligibility for patients with AIDS who often do not live long enough to qualify.

5) For most of the children with HIV infection, the primary health coverage is through Medicaid. We recommend that the Federal government add critically needed services to the minimum benefits which States are required to provide. Specifically, approved drugs, foster care, and home nursing care should be required of all States under Medicaid, with matching Federal funds. The Medicaid waiver program should be expanded to all States, along the lines of the New Jersey pilot program. The private sector should be encouraged to join these waiver programs by contributing funds for the development of case management and out-patient services and by developing innovative coverage strategies.

6) A large number of families of the working poor and the uninsured will fall outside the scope of these coverages. The income eligibility requirements for Medicaid should be altered to allow these families to be covered. As the number of pediatric HIV infections increases, the private sector will have to become more involved, and the Federal government must assume a greater share of the cost of care.

7) A national commission on AIDS, as proposed in pending Congressional legislation, could consider strategies for development of catastrophic health care coverage and would allow for improved accumulation of data better to project future expenses.

WORK GROUP X: EDUCATION AND BEHAVIOR MODIFICATION TO PREVENT HIV INFECTION

DEFINITION OF THE ISSUES:

The issues of how and when to teach children about sex and drug abuse have been with us for decades. We must now add a third issue of when and how to teach about HIV infection and its relationship to sex and drugs. The spread of the AIDS epidemic adds a sense of urgency and fresh controversy to these concerns. The questions are what, when, where, and how to teach children of different age, social, and ethnic backgrounds an understanding of high-risk sexual behavior, the avoidance of drugs, and the prevention of HIV infection.

RECOMMENDATIONS:

The main goal of an AIDS prevention program is to prevent, modify, or eliminate behaviors which may place our children and youth at risk for acquisition of HIV infection. Our recommendations are as follows:

1) A nation-wide, multi-dimensional AIDS Prevention Campaign must be developed and implemented, with adolescents and youth as the targeted group. Specifically, it should include:

a) a social marketing campaign to promote the acceptance and use of condoms as a method of disease prevention. This campaign shall include promotional advertising aimed at all socioeconomic and ethnic groups, as well as steps to increase the availability of condoms to all economic sectors, including free distribution and/or price subsidies;

b) a direct mailing to every household in the nation with a straightforward AIDS prevention message; and

c) the convening of a meeting of innovators in business, advertising, entertainment, and publishing to develop agreement with national leaders to promote AIDS prevention messages through a wide variety of outlets. These include active advertiser support of programs that provide information about risk exposure and transmission from the standpoints of both sexual practices and drug abuse. Sexual abstinence should be portrayed as the preferred method of AIDS prevention. Sexually active people should be presented as caring and responsible adults in their use of condoms to prevent AIDS.

2) A separate office of the Chief of AIDS Operations should be established under the Secretary of Health and headed by an official of national stature with staff and funds commensurate to the importance of AIDS.

3) To be effective, education and prevention strategies must be modified to conform to cultural patterns and beliefs. Information from existing studies on cultural behavior, beliefs, and practices should be examined and incorporated into AIDS prevention strategy. Members of identified cultural communities should be involved in all phases of program planning and implementation.

4) Community-based programs, directed to adults who influence youth and to youths themselves, lend themselves to the development of creative approaches for education. Mechanisms should include educating legislators and other policymakers and utilizing resources directed to reach youth – including peer groups, hotlines, and newsletters – with the coordination and consultation of the youths themselves. Knowledgeable professionals should be trained and their services made available through national organizations.

5) Clergy and denominational leaders should accept responsibility for creating and disseminating material that describes the disease of AIDS, leads to its understanding and control, and provides acceptance and comfort to infected individuals.

6) The Surgeon General should facilitate development of a model HIV infection prevention curriculum with age-appropriate components for pre-kindergarten through college-age students and include teacher-training materials. Schools should place immediate emphasis on education from the junior high through college level, and resources should be developed for counseling students at highest risk. Community-based programs should be integrated with the school educational material. Longer-term school plans should add AIDS prevention education to all school health programs, including health services, clinics, health education classes, and counseling.

7) All AIDS prevention education, whether in-school or out-of-school, should contain two components: a) information and b) skill development. Skills should include communication and coping skills, assertiveness training, self-esteem development, and decision making. We hope the program would help youths to develop a sufficient sense of themselves to postpone intercourse, refuse drug use,

avert sexual abuse, and effectively insist on the use of condoms when becoming sexually active.

8) We recommend Federal, State, and community sponsored programs specifically directed to youth at high risk for HIV exposure: gay and bisexual teenagers, pregnant young women, juvenile male and female prostitutes, runaways, incarcerated youth, and homeless or socially disenfranchised young people. Immediate attention should be directed to the geographic areas of highest HIV prevalence.

9) The current drug avoidance campaign must be expanded to teach intravenous drug users avoidance of AIDS risk. Outreach programs must stress how to avoid drug use and how to gain access to drug treatment programs. Individuals who can't or won't refrain must be taught to avoid sharing needles, how to obtain and use clean needles, and at a minimum how to clean quickly and effectively previously used needles with bleach or alcohol. The communication must be simple, visual, multilingual, and culturally directed.

10) Often, counseling on a repetitive basis is needed to encourage and help maintain behavioral changes. Effective school-community programs must contain the capability for individual and group counseling by experienced professionals.

11) All components of the HIV prevention campaign should include testing and evaluation of implementation, process, and outcome by scientifically designed studies using valid measurement tools.

RESPONSE OF THE SURGEON GENERAL

As Surgeon General, I have neither the power nor the money to implement all of the recommendations of the work groups. I am a catalyst, and my power is that of moral persuasion.

Perhaps the most moving moment of this Workshop came when Mrs. Kushnick said that she was told the death of her son would not count as AIDS. We hope that Mrs. Kushnick and her family recognize how much their courage and their work has made Samuel's life and struggle count very much indeed. We feel that our work here should be dedicated to all the infants and children who – like Samuel – were struck down by pediatric AIDS before we ever recognized the disease. Our work here can begin to help all of the parents and all of the Samuels in the world.

Now I want to respond to the various recommendations of the work groups. Questions about the CDC definition of AIDS are recurrent and are intermingled with questions about and seeming inconsistencies in the numbers of cases of AIDS and the various subcategories created by factors such as age, sex, ethnic group, and presumptive mode of acquisition. The basic confusion comes from the difference between the clinical diagnosis of AIDS (which is made by a physician and is based on clinical acumen and laboratory tests) and the epidemiologic surveillance methods developed and used by CDC. It is absolutely vital to develop accurate methods for both. The ability to diagnose improves with the increase in both our knowledge and our diagnostic tools. To be useful for revealing trends in transmission and incidence as well as for predictions about the future, the CDC definition of AIDS requires consistency. The criteria for inclusion in CDC reporting have changed in the past and will change again as our information becomes more complete. In any case, we should all be careful to make a distinction between clinical diagnosis and epidemiologic reporting.

I acknowledge the recommendations about the CDC guidelines and also those of the American Academy of Pediatrics, and I thank the work groups for doing such a thorough, critical job. I will see that the leadership of both CDC and AAP are promptly made aware of your recommendations.

Certainly, the recommendations of the group working on the natural history of AIDS in children emphasize the importance of comparable longitudinal studies of the disease and its various forms of progression. We expect that the new clinical classification of AIDS published in the *Morbidity and Mortality Weekly Report* (MMWR) will be useful in these efforts and also in the development of multicenter studies of various therapeutic interventions.

The concrete suggestions for research efforts on both the course of the disease and on the treatment protocols of various agents such as ribavirin and AZT will be taken under consideration. In reference to longitudinal studies and information gathering, I can report that Dr. Virginia Anderson, a Public Health Service officer and a participant in this Workshop, has already been detailed by the Service to the Armed Forces Institute of Pathology where she is responsible for a pediatric AIDS registry. I will see that she receives the mailing list of this Workshop in order that she may inform the participants about the registry and how it works.

We are grateful that you have emphasized our ignorance about AIDS in adolescents. The CDC definition of pediatric AIDS ends at age 13; perhaps we have not given sufficient attention to this vulnerable group. We know that 139 teenage cases have been reported. In the *Surgeon General's Report* of October 1986, I did say that adolescents may not know if they are homosexual or will be drug abusers and therefore might not heed or understand messages others might find pertinent. These youngsters must be reached and taught about risk behaviors that expose them to infection with the AIDS virus. We need to know how this virus affects youth during this second period of rapid growth.

We also take note of the specific legal and ethical concerns of drug trials in infants, children, and youth; we are pleased that you have delineated these concerns for us.

Special note is made that many of the children may actually be under the guardianship of a local child welfare agency. We need to help these agencies understand more about pediatric AIDS. This understanding is necessary for the provision of the extra supports these children need and for the awareness of risks and benefits of various treatment protocols. The New Jersey program demonstrates that such a program can be successful.

We should recognize that AIDS can be a possible consequence of child abuse, as some centers dedicated to this problem are already aware. Later this week I will be having the second meeting of a group called "The Health Law Initiative." This is a joint project of the Attorney General and the Surgeon General. We are writing national guidelines which will outline the principles of care for victims of child abuse and their families. The guidelines will also include legal principles relevant to collecting evidence. I will see that the Workshop recommendations are included in those guidelines.

We agree that pilot studies should begin in order to learn the most efficacious methods of newborn detection, including examination of cord blood, careful assessment and follow-up of the newborn, and laboratory distinction between maternal and infant antibodies.

We also agree that the implications of breastmilk transmission are likely to be more critical in developing countries. One cautions that information about AIDS should not cause reduction of breastfeeding when we are attempting to encourage breastfeeding in general. I will bear your strictures in mind, especially when I represent you as delegate to the World Health Organization in the first two weeks of May. I expect this topic will be a part of the heated debate at that time, in view of the past history of that organization over breastmilk substitutes.

Work groups III and V also presented some specific epidemiologic directions for studies by both CDC and National Institutes of Health (NIH). The National Institute for Drug Abuse can be especially useful in providing the knowledge of the connections between the drug-using population and those who work with them. NIDA knows the networks of drug-treatment programs. This knowledge can shed light on the problem of how transmission occurs, how pregnancy affects the woman with HIV infection, and what is the frequency of infected offspring. We acknowledge, however, that studies about drug usage should not be confined to the methadone clinic population—likely to be a biased sample. Of highest priority also is to inform both public and professionals about the outreach programs for drug users in New York, New Jersey, and other States. These programs are successful in improving knowledge and modifying behavior of drug users. Such programs create an immediate need for adequate treatment and prevention programs for addicts, and we must increase the number of slots available.

We believe that women at risk should receive care at a well qualified center before they become pregnant, and an infected woman—and later, her infant—should have the benefit of care by those most experienced. This care should be provided in a regionalized system most suited to the need of each community. The Health Resources and Services Administration (HRSA) has begun to assist four cities in their plans for care for all with HIV infection, and more such projects will be funded this year. These plans include the care of women and children. You advised us that plans must include care in and out of hospital, including counseling and education, psychological support services, foster care, day care, and child development. The suggestion that nurturing homes for small numbers of children be established has struck a responsive chord and is accepted. I will seek to bring together the Division of Maternal and Child Health, the Office of Human Development Services, and the Health Care Financing Administration (HCFA) to pursue this innovative idea.

We have all seen examples of children and youth, as well as siblings and other family members, barred from essential services because of the stigma of AIDS. We have brought participants to this Workshop who could tell us how to be successful in overcoming these barriers and in providing needed services and access for these families. Your recommendations are rich with suggestions we will try to implement. Some of these accommodations are for the public sector, some for the private sector, some for a partnership between the two. I will bring these sectors together to review your recommendations.

For those of you from the various communication media who have developed your Work Group's statements, I hope you note the enormous restraint I have imposed upon myself in answering you. I accept your statements at face value, and I am delighted that you emphasized the need for both clarification and precise, explicit words. During this Workshop, we have heard how many different meanings there are for the same words or phrase. I have long been aware of the problem of semantics in reference to AIDS, and if I have offended anyone, I apologize. Throughout my involvement with AIDS, I have chosen my words about this topic carefully. In spite of the headlines, I have never used the words "safe sex" or "safer sex" and I never used the words "school-based clinic." These buzz words mean very different things to different people. Sometimes I deliberately use words that may seem offensive to some because I am trying to attract the attention of others. For example, when I use the words "innocent victim," it is not to indicate that others are not innocent. It is meant to attract attention, especially of those in our society who would consign all persons with AIDS to outer darkness. I use the term "high risk" because at-risk groups asked me to use it.

I see no reason why we cannot bring together the kinds of people you suggest to write a glossary of terms, not only for the medical profession, but also for the media. We must first achieve consensus before we achieve uniformity, and I will try to catalyse this process.

A project for reaching minority leaders is already underway, and I hope we can announce its effect before very long.

The Surgeon General's Report of October 1986 has already been translated into Spanish and will appear soon. Camera-ready copies will be available for those who wish to reprint the report in Hispanic newspapers or magazines. The Report of this Surgeon General's Workshop will also be printed in Spanish.

We agree that AIDS information should be disseminated by family planning clinics. We already have AIDS Information Programs in all of the ten regions

of the Public Health Service through family planning activities in clinics supported directly or indirectly by PHS funds. We will expand these efforts to the best of our ability.

Catastrophic insurance is something that has always been near to my heart, since I dealt with the tremendously overburdening problems of surgical difficulties in the newborn for over thirty-five years in this very Children's Hospital. Several decades ago, I thought catastrophic insurance was needed for youngsters. As a matter of fact, the very first talk I ever gave in Washington in reference to my present career was on catastrophic insurance for pediatric patients.

With reference to church groups, I have had a cordial reception from all the Protestant groups I have been working with since the first of the year. I have been particularly pleased with the reaction of the National Association of Religious Broadcasters. I spoke to 3,000 of them in Washington last February, and although I chastised them, their response was warm. The most important thing is that many of them who reach a large segment of the radio and television audience are transmitting a message to their constituencies concerning sexuality and concerning the problem of AIDS. One Roman Catholic experiment in Dallas is outstanding. The diocese assembled a curriculum for their junior high and middle school. As I understand it, they gave the courses after school and invited students from the public schools as well. My further information is that the classes were well attended.

The recommendations given by the work group on education are worthy, but difficult to carry out as presented. In the Federal government, we are constantly reminded that we are not in the retail business of education. We do have some model curricula, however. One of those is already a pilot study in Indiana. Other programs from CDC will serve as models to be copied in the days ahead.

Since this past January, I have tried to draw attention to the need for discussion among Federal, State, and municipal health officials and political figures and the private sector to do three things: 1) to assess the cost of AIDS on an annual basis in the future and to consider how the money will be raised, what it will be used for, and who will make that decision; 2) to consider the role of insurance in the cost factors of AIDS; and 3) to plan for alternative types of care for the terminally ill AIDS patient. With the importance of this pediatric workshop, I will stop calling for such actions and will try to effect them as soon as possible.

In the *Surgeon General's Report* of October 1986, I called upon communities to set up task forces to anticipate every phase of community life and of the social fabric impacted by the AIDS epidemic. Many sections of the nation have not yet encountered the problem of pediatric AIDS. In these States, governmental and professional leaders in medicine, public health, education, and human services must begin immediately to plan for what they are going to do when their cities do have a number of HIV-infected children. I will facilitate this process by providing appropriate consultation through our well established network of State, Territorial, and municipal health offices as soon as possible.

Recommendations from this Workshop will be printed in a report within three months. We will ask each of you to inform the Office of the Surgeon General during the next two years about progress on today's recommendations. We have followed this protocol with other workshops, and it has been very successful. We will share subsequent information with all of you so that you will know how your colleagues have fared. You can profit from their successes (or mistakes). We anticipate a follow-up report at the end of two years. The Workshop Report

and all future material will go to every group with potential to respond to your recommendations.

I would like to tell all of you how much I appreciate your presence here. I am sure it is not my gratitude that you seek, but rather – through today's efforts – the gratitude of children yet unborn.

APPENDIX A

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APPENDIX C

GUIDELINES FOR MANAGEMENT OF HIV INFECTION

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APPENDIX D

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APPENDIX E

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MMWR

MORBIDITY AND MORTALITY WEEKLY REPORT

225 Classification System for Human Immunodeficiency Virus (HIV) Infection in Children Under 13 Years of Age

Current Trends

Classification System for Human Immunodeficiency Virus (HIV) Infection in Children Under 13 Years of Age

INTRODUCTION

With the identification of the causative agent of the acquired immunodeficiency syndrome (AIDS), a broad spectrum of clinical manifestations has been attributed to infection with the human immunodeficiency virus (HIV). With the exception of the CDC surveillance definition for AIDS (*1,2*), no standard definitions for other manifestations of HIV infection have been developed for children. Classification systems published to date have been developed primarily to categorize clinical presentations in adult patients and may not be entirely applicable to infants and children (*3-5*).

Physicians from institutions caring for relatively large numbers of HIV-infected children report that only about half of their patients with symptomatic illness related to the infection fulfill the criteria of the CDC surveillance definition for AIDS (*6, 7*).

To develop a classification system for HIV infection in children, CDC convened a panel of consultants* consisting of clinicians experienced in the diagnosis and management of children with HIV infection; public health physicians; representatives from the American Academy of Pediatrics, the Council of State and Territorial Epidemiologists, the Association for Maternal Child Health and Crippled Children's Programs, the National Institute on Drug Abuse/Alcohol, Drug Abuse and Mental Health Administration, the National Institute of Allergy and Infectious Diseases/National Institutes of Health, and the Division of Maternal and Child Health/Health Resources and Services Administration; and CDC.

GOALS AND OBJECTIVES OF THE CLASSIFICATION SYSTEM

The system was designed primarily for public health purposes, including epidemiologic studies, disease surveillance, prevention programs, and health-care planning and policy. The panel attempted to devise a simple scheme that could be subdivided as needed for different purposes.

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HIV Infection – Continued

DEFINITION OF HIV INFECTION IN CHILDREN (Table 1)

Ideally, HIV infection in children is identified by the presence of the virus in blood or tissues, confirmed by culture or other laboratory detection methods. However, current tests—including culture—for detecting the virus or its antigens are not standardized and are not readily available. Detection of specific antibody to the virus is a sensitive and specific indicator of HIV infection in adults, since the majority of adults with antibody have had culture evidence of infection (*8-10*). Similar studies involving children have not been reported. Also, the presence of passively transferred maternal antibody in infants limits the interpretation of a positive antibody test result in this age group. Most of the consultants believed that passively transferred maternal HIV antibody could sometimes persist for up to 15 months. For this reason, two definitions for infection in children are needed: one for infants and children up to 15 months of age who have been exposed to their infected mothers perinatally, and another for older children with perinatal infection and for infants and children of all ages acquiring the virus through other means.

Infants and children under 15 months of age with perinatal infection—Infection in infants and children up to 15 months of age who were exposed to infected mothers in the perinatal period may be defined by one or more of the following: 1) the identification of the virus in blood or tissues, 2) the presence of HIV antibody as indicated by a repeatedly reactive screening test (e.g., enzyme immunoassay) plus a positive confirmatory test (e.g., Western blot, immunofluorescence assay) in an infant or child who has abnormal immunologic test results indicating both humoral and cellular immunodeficiency (increased immunoglobulin levels, depressed T4 [T-helper] absolute cell count, absolute lymphopenia, decreased T4/T8 ratio) and who meets the requirements of one or more of the subclasses listed under class P-2 (described below), or 3) the confirmation that a child's symptoms meet the previously published CDC case definition for pediatric AIDS (*1,2*).

The infection status of other perinatally exposed seropositive infants and children up to 15 months of age who lack one of the above immunologic or clinical criteria is indeterminate. These infants should be followed up for HIV-related illness, and they should be tested at regu-

TABLE 1. Summary of the definition of HIV infection in children

Infants and children under 15 months of age with perinatal infection

1) Virus in blood or tissues
   or
2) HIV antibody
   and
   evidence of both cellular and humoral immune deficiency
   and
   one or more categories in Class P-2
   or
3) Symptoms meeting CDC case definition for AIDS

Older children with perinatal infection and children with HIV infection acquired through other modes of transmission

1) Virus in blood or tissues
   or
2) HIV antibody
   or
3) Symptoms meeting CDC case definition for AIDS

HIV Infection – Continued

lar intervals for persistence of antibody to HIV. Infants and children who become seronegative, are virus-culture negative (if blood or tissue samples are cultured), and continue to have no clinical or laboratory-confirmed abnormalities associated with HIV infection are unlikely to be infected.

Older children with perinatal infection and children with HIV infection acquired through other modes of transmission—HIV infection in these children is defined by one or more of the following: 1) the identification of virus in blood or tissues, 2) the presence of HIV antibody (positive screening test plus confirmatory test) regardless of whether immunologic abnormalities or signs or symptoms are present, or 3) the confirmation that the child's symptoms meet the previously published CDC case definition for pediatric AIDS (*1,2*).

These definitions apply to children under 13 years of age. Persons 13 years of age and older should be classified according to the adult classification system (*3*).

CLASSIFICATION SYSTEM (Table 2)

Children fulfilling the definition of HIV infection discussed above may be classified into one of two mutually exclusive classes based on the presence or absence of clinical signs and symptoms (Table 2). Class Pediatric-1 (P-1) is further subcategorized on the basis of the presence or absence of immunologic abnormalities, whereas Class P-2 is subdivided by specific disease patterns. Once a child has signs and symptoms and is therefore classified in P-2, he or she should not be reassigned to class P-1 if signs and symptoms resolve.

Perinatally exposed infants and children whose infection status is indeterminate are classified into class P-0.

Class P-0. Indeterminate infection. Includes perinatally exposed infants and children up to 15 months of age who cannot be classified as definitely infected according to the above definition but who have antibody to HIV, indicating exposure to a mother who is infected.

Class P-1. Asymptomatic infection. Includes patients who meet one of the above defini-

TABLE 2. Summary of the classification of HIV infection in children under 13 years of age

Class P-0. Indeterminate infection

Class P-1. Asymptomatic infection

- Subclass A. Normal immune function
- Subclass B. Abnormal immune function
- Subclass C. Immune function not tested

Class P-2. Symptomatic infection

- Subclass A. Nonspecific findings
- Subclass B. Progressive neurologic disease
- Subclass C. Lymphoid interstitial pneumonitis
- Subclass D. Secondary infectious diseases
  - Category D-1. Specified secondary infectious diseases listed in the CDC surveillance definition for AIDS
  - Category D-2. Recurrent serious bacterial infections
  - Category D-3. Other specified secondary infectious diseases
- Subclass E. Secondary cancers
  - Category E-1. Specified secondary cancers listed in the CDC surveillance definition for AIDS
  - Category E-2. Other cancers possibly secondary to HIV infection
- Subclass F. Other diseases possibly due to HIV infection

HIV Infection – Continued

tions for HIV infection but who have had no previous signs or symptoms that would have led to classification in Class P-2.

These children may be subclassified on the basis of immunologic testing. This testing should include quantitative immunoglobulins, complete blood count with differential, and T-lymphocyte subset quantitation. Results of functional testing of lymphocytes (mitogens, such as pokeweed) may also be abnormal in HIV-infected children, but it is less specific in comparison with immunoglobulin levels and lymphocyte subset analysis, and it may be impractical.

Subclass A - Normal immune function. Includes children with no immune abnormalities associated with HIV infection.

Subclass B - Abnormal immune function. Includes children with one or more of the commonly observed immune abnormalities associated with HIV infection, such as hypergammaglobulinemia, T-helper (T4) lymphopenia, decreased T-helper/T-suppressor (T4/T8) ratio, and absolute lymphopenia. Other causes of these abnormalities must be excluded.

Subclass C - Not tested. Includes children for whom no or incomplete (see above) immunologic testing has been done.

Class P-2. Symptomatic infection. Includes patients meeting the above definitions for HIV infection and having signs and symptoms of infection. Other causes of these signs and symptoms should be excluded. Subclasses are defined based on the type of signs and symptoms that are present. Patients may be classified in more than one subclass.

Subclass A - Nonspecific findings. Includes children with two or more unexplained nonspecific findings persisting for more than 2 months, including fever, failure-to-thrive or weight loss of more than 10% of baseline, hepatomegaly, splenomegaly, generalized lymphadenopathy (lymph nodes measuring at least 0.5 cm present in two or more sites, with bilateral lymph nodes counting as one site), parotitis, and diarrhea (three or more loose stools per day) that is either persistent or recurrent (defined as two or more episodes of diarrhea accompanied by dehydration within a 2-month period).

Subclass B - Progressive neurologic disease. Includes children with one or more of the following progressive findings: 1) loss of developmental milestones or intellectual ability, 2) impaired brain growth (acquired microcephaly and/or brain atrophy demonstrated on computerized tomographic scan or magnetic resonance imaging scan), or 3) progressive symmetrical motor deficits manifested by two or more of these findings: paresis, abnormal tone, pathologic reflexes, ataxia, or gait disturbance.

Subclass C - Lymphoid interstitial pneumonitis. Includes children with a histologically confirmed pneumonitis characterized by diffuse interstitial and peribronchiolar infiltration of lymphocytes and plasma cells and without identifiable pathogens, or, in the absence of a histologic diagnosis, a chronic pneumonitis—characterized by bilateral reticulonodular interstitial infiltrates with or without hilar lymphadenopathy—present on chest X-ray for a period of at least 2 months and unresponsive to appropriate antimicrobial therapy. Other causes of interstitial infiltrates should be excluded, such as tuberculosis, *Pneumocystis carinii* pneumonia, cytomegalovirus infection, or other viral or parasitic infections.

Subclass D - Secondary infectious diseases. Includes children with a diagnosis of an infectious disease that occurs as a result of immune deficiency caused by infection with HIV.

Category D-1. Includes patients with secondary infectious disease due to one of the specified infectious diseases listed in the CDC surveillance definition for AIDS: *Pneumocystis carinii* pneumonia; chronic cryptosporidiosis; disseminated toxoplasmosis with onset after 1 month of age; extra-intestinal strongyloidiasis; chronic isosporiasis; candidiasis (esophageal, bronchial, or pulmonary); extrapulmonary cryptococco-

HIV Infection – Continued

sis; disseminated histoplasmosis; noncutaneous, extrapulmonary, or disseminated mycobacterial infection (any species other than leprae); cytomegalovirus infection with onset after 1 month of age; chronic mucocutaneous or disseminated herpes simplex virus infection with onset after 1 month of age; extrapulmonary or disseminated coccidioidomycosis; nocardiosis; and progressive multifocal leukoencephalopathy.

Category D-2. Includes patients with unexplained, recurrent, serious bacterial infections (two or more within a 2-year period) including sepsis, meningitis, pneumonia, abscess of an internal organ, and bone/joint infections.

Category D-3. Includes patients with other infectious diseases, including oral candidiasis persisting for 2 months or more, two or more episodes of herpes stomatitis within a year, or multidermatomal or disseminated herpes zoster infection.

Subclass E - Secondary cancers. Includes children with any cancer described below in categories E-1 and E-2.

Category E-1. Includes patients with the diagnosis of one or more kinds of cancer known to be associated with HIV infection as listed in the surveillance definition of AIDS and indicative of a defect in cell-mediated immunity: Kaposi's sarcoma, B-cell non-Hodgkin's lymphoma, or primary lymphoma of the brain.

Category E-2. Includes patients with the diagnosis of other malignancies possibly associated with HIV infection.

Subclass F - Other diseases. Includes children with other conditions possibly due to HIV infection not listed in the above subclasses, such as hepatitis, cardiopathy, nephropathy, hematologic disorders (anemia, thrombocytopenia), and dermatologic diseases.

Reported by: AIDS Program, Center for Infectious Diseases, CDC.

Editorial Note: This classification system is based on present knowledge and understanding of pediatric HIV infection and may need to be revised as new information becomes available. New diagnostic tests, particularly antigen detection tests and HIV-specific IgM tests, may lead to a better definition of HIV infection in infants and children. Information from several natural history studies currently under way may necessitate changes in the subclasses based on clinical signs and symptoms.

A definitive diagnosis of HIV infection in perinatally exposed infants and children under 15 months of age can be difficult. The infection status of these HIV-seropositive infants and children who are asymptomatic without immune abnormalities cannot be determined unless virus culture or other antigen-detection tests are positive. Negative virus cultures do not necessarily mean the child is not infected, since the sensitivity of the culture may be low. Decreasing antibody titers have been helpful in diagnosing other perinatal infections, such as toxoplasmosis and cytomegalovirus. However, the pattern of HIV-antibody production in infants is not well defined. At present, close follow-up of these children (Class P-0) for signs and symptoms indicative of HIV infection and/or persistence of HIV antibody is recommended.

The parents of children with HIV infection should be evaluated for HIV infection, particularly the mother. The child is often the first person in such families to become symptomatic. When HIV infection in a child is suspected, a careful history should be taken to elicit possible risk factors for the parents and the child. Appropriate laboratory tests, including HIV serology, should be offered. If the mother is seropositive, other children should be evaluated regarding their risk of perinatally acquired infection. Intrafamilial transmission, other than perinatal or sexual, is extremely unlikely. Identification of other infected family members allows for appropriate medical care and prevention of transmission to sexual partners and future children (*11,12*).

HIV Infection -- Continued

The nonspecific term AIDS-related complex has been widely used to describe symptomatic HIV-infected children who do not meet the CDC case definition for AIDS. This classification system categorizes these children more specifically under Class P-2.

The development and publication of this classification system does not imply any immediate change in the definition of pediatric AIDS used by CDC for reporting purposes (*1,2*). Changes in this definition require approval by state and local health departments. However, changes in the definition for reporting cases have been proposed by CDC and are awaiting state and local approval.

Written comments are encouraged. They should be mailed to the AIDS Program, Center for Infectious Diseases, Centers for Disease Control, Atlanta, GA 30333.

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MMWR

MORBIDITY AND MORTALITY WEEKLY REPORT

Current Trends

Education and Foster Care of Children Infected with Human T-Lymphotropic Virus Type III/ Lymphadenopathy-Associated Virus

The information and recommendations contained in this document were developed and compiled by CDC in consultation with individuals appointed by their organizations to represent the Conference of State and Territorial Epidemiologists, the Association of State and Territorial Health Officers, the National Association of County Health Officers, the Division of Maternal and Child Health (Health Resources and Services Administration), the National Association for Elementary School Principals, the National Association of State School Nurse Consultants, the National Congress of Parents and Teachers, and the Children's Aid Society. The consultants also included the mother of a child with acquired immunodeficiency syndrome (AIDS), a legal advisor to a state education department, and several pediatricians who are experts in the field of pediatric AIDS. This document is made available to assist state and local health and education departments in developing guidelines for their particular situations and locations.

These recommendations apply to all children known to be infected with human T-lymphotropic virus type III/lymphadenopathy-associated virus (HTLV-III/LAV). This includes children with AIDS as defined for reporting purposes (Table 1); children who are diagnosed by their physicians as having an illness due to infection with HTLV-III/LAV but who do not meet the case definition; and children who are asymptomatic but have virologic or serologic evidence of infection with HTLV-III/LAV. These recommendations do not apply to siblings of infected children unless they are also infected.

BACKGROUND

The Scope of the Problem. As of August 20, 1985, 183 of the 12,599 reported cases of AIDS in the United States were among children under 18 years of age. This number is expected to double in the next year. Children with AIDS have been reported from 23 states, the District of Columbia, and Puerto Rico, with 75% residing in New York, California, Florida, and New Jersey.

The 183 AIDS patients reported to CDC represent only the most severe form of HTLV-III/LAV infection, i.e., those children who develop opportunistic infections or malignancies (Table 1). As in adults with HTLV-III/LAV infection, many infected children may have milder illness or may be asymptomatic.

Legal Issues. Among the legal issues to be considered in forming guidelines for the education and foster care of HTLV-III/LAV-infected children are the civil rights aspects of public

HTLV-III/LAV – Continued

TABLE 1. Provisional case definition for acquired immunodeficiency syndrome (AIDS) surveillance of children

For the limited purposes of epidemiologic surveillance, CDC defines a case of pediatric acquired immunodeficiency syndrome (AIDS) as a child who has had:

1. A reliably diagnosed disease at least moderately indicative of underlying cellular immunodeficiency, and
2. No known cause of underlying cellular immunodeficiency or any other reduced resistance reported to be associated with that disease.

The diseases accepted as sufficiently indicative of underlying cellular immunodeficiency are the same as those used in defining AIDS in adults. In the absence of these opportunistic diseases, a histologically confirmed diagnosis of chronic lymphoid interstitial pneumonitis will be considered indicative of AIDS unless test(s) for HTLV-III/LAV are negative. Congenital infections, e.g., toxoplasmosis or herpes simplex virus infection in the first month after birth or cytomegalovirus infection in the first 6 months after birth must be exluded.

Specific conditions that must be excluded in a child are:

1. Primary immunodeficiency diseases—severe combined immunodeficiency, DiGeorge syndrome, Wiskott-Aldrich syndrome, ataxia-telangiectasia, graft versus host disease, neutropenia, neutrophil function abnormality, agammaglobulinemia, or hypogammaglobulinemia with raised IgM.
2. Secondary immunodeficiency associated with immunosuppressive therapy, lymphoreticular malignancy, or starvation.

school attendance, the protections for handicapped children under 20 U.S.C. 1401 et seq. and 29 U.S.C. 794, the confidentiality of a student's school record under state laws and under 20 U.S.C. 1232g, and employee right-to-know statutes for public employees in some states.

Confidentiality Issues. The diagnosis of AIDS or associated illnesses evokes much fear from others in contact with the patient and may evoke suspicion of life styles that may not be acceptable to some persons. Parents of HTLV-III/LAV-infected children should be aware of the potential for social isolation should the child's condition become known to others in the care or educational setting. School, day-care, and social service personnel and others involved in educating and caring for these children should be sensitive to the need for confidentiality and the right to privacy in these cases.

ASSESSMENT OF RISKS

Risk Factors for Acquiring HTLV-III/LAV Infection and Transmission. In adults and adolescents, HLTV-III/LAV is transmitted primarily through sexual contact (homosexual or heterosexual) and through parenteral exposure to infected blood or blood products. HTLV-III/LAV has been isolated from blood, semen, saliva, and tears but transmission has not been documented from saliva and tears. Adults at increased risk for acquiring HTLV-III/LAV include homosexual/bisexual men, intravenous drug abusers, persons transfused with contaminated blood or blood products, and sexual contacts of persons with HTLV-III/LAV infection or in groups at increased risk for infection.

The majority of infected children acquire the virus from their infected mothers in the perinatal period (*1-4*). In utero or intrapartum transmission are likely, and one child reported from Australia apparently acquired the virus postnatally, possibly from ingestion of breast milk (*5*). Children may also become infected through transfusion of blood or blood products that contain the virus. Seventy percent of the pediatric cases reported to CDC occurred among children whose parent had AIDS or was a member of a group at increased risk of acquiring HTLV-III/LAV infection; 20% of the cases occurred among children who had received blood or blood products; and for 10%, investigations are incomplete.

HTLV-III/LAV – Continued

Risk of Transmission in the School, Day-Care or Foster-Care Setting. None of the identified cases of HTLV-III/LAV infection in the United States are known to have been transmitted in the school, day-care, or foster-care setting or through other casual person-to-person contact. Other than the sexual partners of HTLV-III/LAV-infected patients and infants born to infected mothers, none of the family members of the over 12,000 AIDS patients reported to CDC have been reported to have AIDS. Six studies of family members of patients with HTLV-III/LAV infection have failed to demonstrate HTLV-III/LAV transmission to adults who were not sexual contacts of the infected patients or to older children who were not likely at risk from perinatal transmission (*6-11*).

Based on current evidence, casual person-to-person contact as would occur among schoolchildren appears to pose no risk. However, studies of the risk of transmission through contact between younger children and neurologically handicapped children who lack control of their body secretions are very limited. Based on experience with other communicable diseases, a theoretical potential for transmission would be greatest among these children. It should be emphasized that any theoretical transmission would most likely involve exposure of open skin lesions or mucous membranes to blood and possibly other body fluids of an infected person.

Risks to the Child with HTLV-III/LAV Infection. HTLV-III/LAV infection may result in immunodeficiency. Such children may have a greater risk of encountering infectious agents in a school or day-care setting than at home. Foster homes with multiple children may also increase the risk. In addition, younger children and neurologically handicapped children who may display behaviors such as mouthing of toys would be expected to be at greater risk for acquiring infections. Immunodepressed children are also at greater risk of suffering severe complications from such infections as chickenpox, cytomegalovirus, tuberculosis, herpes simplex, and measles. Assessment of the risk to the immunodepressed child is best made by the child's physician who is aware of the child's immune status. The risk of acquiring some infections, such as chickenpox, may be reduced by prompt use of specific immune globulin following a known exposure.

RECOMMENDATIONS

1. Decisions regarding the type of educational and care setting for HTLV-III/LAV-infected children should be based on the behavior, neurologic development, and physical condition of the child and the expected type of interaction with others in that setting. These decisions are best made using the team approach including the child's physician, public health personnel, the child's parent or guardian, and personnel associated with the proposed care or educational setting. In each case, risks and benefits to both the infected child and to others in the setting should be weighed.
2. For most infected school-aged children, the benefits of an unrestricted setting would outweigh the risks of their acquiring potentially harmful infections in the setting and the apparent nonexistent risk of transmission of HTLV-III/LAV. These children should be allowed to attend school and after-school day-care and to be placed in a foster home in an unrestricted setting.
3. For the infected preschool-aged child and for some neurologically handicapped children who lack control of their body secretions or who display behavior, such as biting, and those children who have uncoverable, oozing lesions, a more restricted environment is advisable until more is known about transmission in these settings. Children infected with HTLV-III/LAV should be cared for and educated in settings that minimize exposure of other children to blood or body fluids.

HTLV-III/LAV – Continued

4. Care involving exposure to the infected child's body fluids and excrement, such as feeding and diaper changing, should be performed by persons who are aware of the child's HTLV-III/LAV infection and the modes of possible transmission. In any setting involving an HTLV-III/LAV-infected person, good handwashing after exposure to blood and body fluids and before caring for another child should be observed, and gloves should be worn if open lesions are present on the caretaker's hands. Any open lesions on the infected person should also be covered.
5. Because other infections in addition to HTLV-III/LAV can be present in blood or body fluids, all schools and day-care facilities, regardless of whether children with HTLV-III/LAV infection are attending, should adopt routine procedures for handling blood or body fluids. Soiled surfaces should be promptly cleaned with disinfectants, such as household bleach (diluted 1 part bleach to 10 parts water). Disposable towels or tissues should be used whenever possible, and mops should be rinsed in the disinfectant. Those who are cleaning should avoid exposure of open skin lesions or mucous membranes to the blood or body fluids.
6. The hygienic practices of children with HTLV-III/LAV infection may improve as the child matures. Alternatively, the hygienic practices may deteriorate if the child's condition worsens. Evaluation to assess the need for a restricted environment should be performed regularly.
7. Physicians caring for children born to mothers with AIDS or at increased risk of acquiring HTLV-III/LAV infection should consider testing the children for evidence of HTLV-III/LAV infection for medical reasons. For example, vaccination of infected children with live virus vaccines, such as the measles-mumps-rubella vaccine (MMR), may be hazardous. These children also need to be followed closely for problems with growth and development and given prompt and aggressive therapy for infections and exposure to potentially lethal infections, such as varicella. In the event that an antiviral agent or other therapy for HTLV-III/LAV infection becomes available, these children should be considered for such therapy. Knowledge that a child is infected will allow parents and other caretakers to take precautions when exposed to the blood and body fluids of the child.
8. Adoption and foster-care agencies should consider adding HTLV-III/LAV screening to their routine medical evaluations of children at increased risk of infection before placement in the foster or adoptive home, since these parents must make decisions regarding the medical care of the child and must consider the possible social and psychological effects on their families.
9. Mandatory screening as a condition for school entry is not warranted based on available data.
10. Persons involved in the care and education of HTLV-III/LAV-infected children should respect the child's right to privacy, including maintaining confidential records. The number of personnel who are aware of the child's condition should be kept at a minimum needed to assure proper care of the child and to detect situations where the potential for transmission may increase (e.g., bleeding injury).
11. All educational and public health departments, regardless of whether HTLV-III/LAV-infected children are involved, are strongly encouraged to inform parents, children, and educators regarding HTLV-III/LAV and its transmission. Such education would greatly assist efforts to provide the best care and education for infected children while minimizing the risk of transmission to others.

HTLV-III/LAV – Continued

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"Until we find a vaccine or cure, the only way to stop the spread of AIDS is through education."

"The public must become comfortable with the knowledge that quarantine is not the answer to preventing the spread of AIDS. Education is."